In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: October 31, 2023

LISA L. ARREDONDO,	*	PUBLISHED
	*	
Petitioner,	*	No. 18-1782V
	*	
v.	*	Special Master Nora Beth Dorsey
	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Entitlement; Influenza ("Flu") Vaccine; Bell's Palsy.
	*	
Respondent.	*	
	*	

Lisa Roquemore, Law Office of Lisa A. Roquemore, Rancho Santa Margarita, CA, for Petitioner.
Bridget Corridon, U.S. Department of Justice, Washington, DC, for Respondent.

RULING ON ENTITLEMENT[1]

I. INTRODUCTION

On November 19, 2018, Lisa L. Arredondo ("Petitioner") filed a petition for compensation under the National Vaccine Injury Compensation Program ("Vaccine Act" or "the

[1] Because this Ruling contains a reasoned explanation for the action in this case, the undersigned is required to post it on the United States Court of Federal Claims' website and/or at https://www.govinfo.gov/app/collection/uscourts/national/cofc in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2018) (Federal Management and Promotion of Electronic Government Services). **This means the Ruling will be available to anyone with access to the Internet.** In accordance with Vaccine Rule 18(b), Petitioner has 14 days to identify and move to redact medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. If, upon review, the undersigned agrees that the identified material fits within this definition, the undersigned will redact such material from public access.

Program"), 42 U.S.C. § 300aa-10 et seq. (2018).[2] Petitioner alleges that she suffered Bell's palsy as the result of an influenza ("flu") vaccination administered on September 21, 2017. Petition at 2 (ECF No. 1). Respondent argued against compensation, stating that "[P]etitioner is not entitled to an award under the [Vaccine] Act." Respondent's Report ("Resp. Rept.") at 4 (ECF No. 21).

After carefully analyzing and weighing the evidence presented in this case in accordance with the applicable legal standards, the undersigned finds that Petitioner has provided preponderant evidence that her flu vaccine caused her Bell's palsy, satisfying Petitioner's burden of proof under Althen v. Secretary of Health & Human Services, 418 F.3d 1274, 1280 (Fed. Cir. 2005). Accordingly, Petitioner is entitled to compensation.

II. ISSUES TO BE DECIDED

Diagnosis is not at issue. Joint Prehearing Submission, filed Sept. 13, 2022 at 1 (ECF No. 75). The parties stipulated that Petitioner received a flu vaccine on September 21, 2017, and that onset of her symptoms, consistent with Bell's palsy, was October 1, 2017. Id.

The central issue is whether Petitioner has provided preponderant evidence of causation for all three Althen prongs. Joint Prehearing Submission at 2. Petitioner asserts that she has met her burden under the Althen prongs. Petitioner's Prehearing Brief ("Pet. Br."), filed Sept. 6, 2022, at 25-32 (ECF No. 68). Respondent disagrees and argues that Petitioner failed to submit preponderant evidence that her flu vaccine more likely than not caused her Bell's palsy. Resp. Prehearing Br. ("Resp. Br."), filed Sept. 27, 2022, at 15-31 (ECF No. 78).

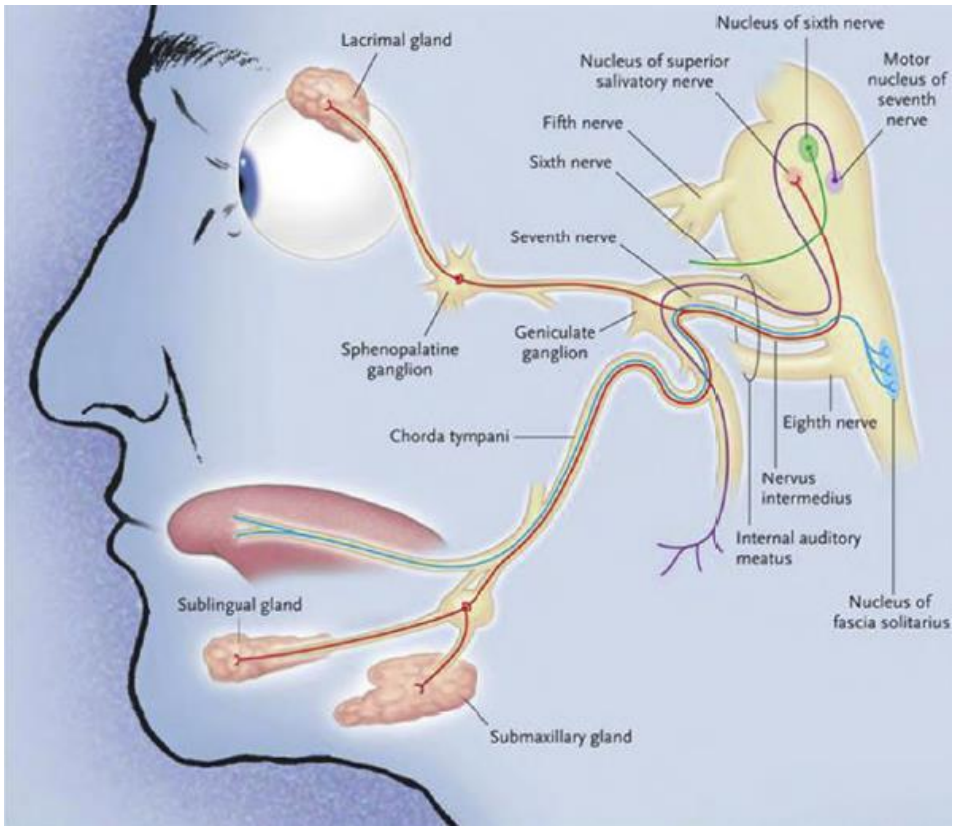
III. BACKGROUND

A. Medical Terminology

Bell's palsy is defined as "unilateral facial paralysis of sudden onset, due to [a] lesion of the facial nerve[,] [] resulting in characteristic distortion of the face." Bell Palsy, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=95779 (last visited Oct. 23, 2023). Bell's palsy is considered an "idiopathic peripheral nerve palsy involving

[2] The National Vaccine Injury Compensation Program is set forth in Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755, codified as amended, 42 U.S.C. §§ 300aa-10 to -34 (2018) ("Vaccine Act" or "the Act"). All citations in this Ruling to individual sections of the Vaccine Act are to 42 U.S.C.A. § 300aa.

the facial nerve." Pet. Exhibit ("Ex.") 19 at 1.[3] The facial nerve (seventh cranial nerve)[4] "travels through a narrow, bony canal . . . in the skull, beneath the ear, to the muscles on each side of the face." Pet. Ex. 17 at 1.[5] It innervates muscles on the face that "control eye blinking and closing, and facial expressions like smiling and frowning." Id. The facial nerve also "carries nerve impulses to the . . . the tear glands, the saliva glands, and the muscles of a small bone in the middle ear" as well as the tongue. Id. When the "function of the facial nerve is disrupted," facial paralysis or weakness occurs. Id.



[3] A. Greco et al., Bell's Palsy and Autoimmunity, 12 Autoimmunity Rev. 323 (2012).

[4] The facial nerve, or seventh cranial nerve, "consist[s] of two roots: a large motor root, which supplies the muscles of facial expression, and a smaller root, the nervus intermedius." Nervus Facialis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=92293 (last visited Oct. 19, 2023). The nervus intermedius, or intermediate nerve, "joins the main root at, or merges with, the geniculate ganglion at the geniculum of the facial nerve; it contributes parasympathetic and special sensory fibers to the facial nerve." Nervus Intermedius, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=92313 (last visited Oct. 19, 2023).

[5] Bell's Palsy Fact Sheet, NINDS, https://www.ninds.nih.gov/bells-palsy-fact-sheet (last modified June 6, 2018).

Pet. Ex. 19 at 2.

Although Bell's palsy is a well-known and common disease, its etiology remains unclear. Pet. Ex. 73 at 1;[6] Pet. Ex. 68 at 1.[7] However, autoimmune, inflammatory, and infectious etiologies have been postulated. Pet. Ex. 19 at 1. Bell's palsy has "been associated with [flu] or a flu-like illness." Pet. Ex. 17 at 1.

B. Procedural History

Petitioner filed her petition on November 19, 2018 and filed medical records[8] and an expert report from Dr. Lawrence Steinman the following day. Petition; Pet. Exs. 1-36. On August 19, 2019, Respondent filed a Rule 4(a) Report providing the abbreviated facts of the case but indicated that medical personnel at the Division of Injury Compensation Programs ("DICP") had not yet been able to review the claim and offer an opinion as to Respondent's position. Resp. Rept. at 3. Respondent stated that "[P]etitioner is not entitled to an award under the [Vaccine] Act" but was awaiting "DICP's input prior to making a determination whether an informal resolution is warranted in this case." Id. at 4. Thereafter, Respondent filed a status report indicating his intent to defend the claim. Resp. Status Rept., filed Oct. 31, 2019 (ECF No. 24) ("[R]espondent is not interested in engaging in settlement discussions and intends to file a responsive expert report.").

The matter was reassigned to the undersigned on October 1, 2019. Notice of Reassignment dated Oct. 1, 2019 (ECF No. 23). On March 23, 2020, Respondent filed expert reports from Dr. Brian Callaghan and Dr. J. Lindsay Whitton. Resp. Exs. A, C. Petitioner filed a responsive declaration on May 25, 2020. Pet. Ex. 46. On July 15, 2020, Petitioner filed a supplemental expert report from Dr. Steinman. Pet. Ex. 47. And Respondent filed a supplemental expert report from Dr. Whitton on September 20, 2020. Resp. Ex. E.

Pursuant to the parties' request, the undersigned held a Rule 5 status conference on December 2, 2020. Rule 5 Order dated Dec. 2, 2020 (ECF No. 45); see Pet. Joint Status Rept., filed Oct. 21, 2020 (ECF No. 43). The undersigned preliminarily found Petitioner's proper

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[6] Weigong Zhou et al., A Potential Signal of Bell's Palsy After Parenteral Inactivated Influenza Vaccines: Reports to the Vaccine Adverse Event Reporting System (VAERS) United States, 1991-2001, 13 Pharmacoepidemiology & Drug Safety 505 (2004).

[7] Cheng-Hsiu Chou et al., Bell's Palsy Associated with Influenza Vaccination: Two Case Reports, 25 Vaccine 2839 (2007).

[8] Petitioner filed additional medical records throughout the course of litigation.

diagnosis was Bell's palsy, not Ramsay Hunt syndrome.[9] Rule 5 Order at 2. The undersigned made a preliminary finding that Petitioner had provided preponderant evidence of causation based on the Althen prongs and posited "that if this case went to a hearing, she would probably find in favor of [P]etitioner." Id. at 3. However, given the risk of litigation, she recommended that "this case should be resolved by settlement." Id.

The parties entertained settlement until March 2021. See ECF Nos. 49-50, 52. However, after consideration, Respondent did not wish to engage in further settlement discussions. Resp. Status Rept., filed Mar. 9, 2021 (ECF No. 52). At a status conference on April 15, 2021, Petitioner conveyed her preference to resolve the case through an entitlement hearing. Order dated Apr. 15, 2021 (ECF No. 54); see also Pet. Joint Status Rept., filed May 4, 2021 (ECF No. 55).

Petitioner filed a supplemental expert report from Dr. Steinman on August 24, 2022. Pet. Ex. 75. An entitlement hearing was held October 18-19, 2022. Order dated Oct. 19, 2022 (ECF No. 80). Petitioner, Dr. Steinman, Dr. Callaghan, and Dr. Whitton testified at the hearing. Transcript ("Tr.") 3, 145. On October 24, 2022, Petitioner filed a supplemental expert report from Dr. Steinman and supporting medical literature. Pet. Exs. 83-86.

At a status conference on December 20, 2022, it was agreed that post-hearing briefs were not necessary. Order dated Dec. 20, 2022 (ECF No. 86). However, given that Dr. Steinman provided a post-hearing explanation on an issue, Respondent requested the opportunity to file a responsive opinion and Petitioner further requested the opportunity to offer a rebuttal opinion. Id. Respondent filed a supplemental expert report by Dr. Callaghan on January 31, 2023, and Petitioner filed an opinion letter from Dr. Robert P. Lisak on February 8, 2023. Resp. Ex. G; Pet. Ex. 91. On March 31, 2023, Respondent filed a status report in response to Dr. Lisak's letter and indicated the record was complete for a ruling. Resp. Status Rept., filed Mar. 1, 2023, at 3 n.3, 6 (ECF No. 90). The same day, Petitioner also filed a status report confirming the record was complete for a ruling. Pet. Status Rept., filed Mar. 1, 2023 (ECF No. 91).

This matter is now ripe for adjudication.

C. Medical History

Petitioner is a registered nurse who received her flu vaccination due to work requirements; she received the quadrivalent Flucelvax flu vaccine in her left deltoid on September 21, 2017. Pet. Ex. 1 at 1; Tr. 7.

[9] Ramsay Hunt syndrome is "herpes zoster involving the facial and vestibulocochlear nerves, often associated with transitory ipsilateral facial paralysis and herpetic vesicles of the external ear or tympanic membrane." Ramsay Hunt Syndrome, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=111266 (last visited Oct. 19, 2023). Because the parties stipulated that Petitioner was properly diagnosed with Bell's palsy, the undersigned will not discuss the expert opinions pertaining to Ramsay Hunt in this Ruling. See Joint Prehearing Submission at 1.

Thirteen days later, on October 4, 2017, Petitioner presented to her primary care physician ("PCP") at South Alamo Medical Group with paresthesia, "drooping right eye," and pain in her ear that started three days prior. Pet. Ex. 3 at 27. Associated symptoms included "difficulty closing eye, drooping lower eyelid, facial muscle weakness[,] and pain near the ear." Id. Prior history of chickenpox was "unknown." Id. Physical examination did not reveal any rash or vesicles on her face or around her right ear. Id. at 29. Neurological examination revealed the fifth (V)[10] and seventh (VII) cranial nerves were abnormal on the right side. Id. Petitioner was diagnosed with paresthesia and Bell's palsy, prescribed acyclovir[11] and steroids, and magnetic resonance imaging ("MRI") was ordered. Id. at 29-30. A brain MRI performed without contrast on October 9 showed "[n]o significant intracranial abnormality." Id. at 32.

On October 10, 2017, Petitioner's employer submitted a report to the Vaccine Adverse Event Reporting System ("VAERS")[12] on her behalf. Pet. Ex. 2. The adverse event was described as facial paralysis and neck pain following the flu vaccine. Id. at 3. It reported that Petitioner "woke up the night of [October 1, 2017] with pain in neck and left sided drooping[13] which ha[d] not yet resolved." Id. For the report, Petitioner reported to her employer that she was diagnosed with Bell's palsy. Id.

Petitioner returned to her PCP on October 11, 2017 "for evaluation of Bell's palsy with inability to smile and pain in right ear." Pet. Ex. 3 at 33. Associated symptoms included difficulty drinking, eating, and speaking, facial muscle weakness, "and pain near the ear, but no blisters in or near the ear,[14] difficulty closing eye, drooping lower eyelid, drooling, hearing loss,

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[10] The fifth cranial nerve, or trigeminal nerve, "is sensory in supplying the face, teeth, mouth, and nasal cavity, and motor in supplying the muscles of mastication." Nervus Trigeminus, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=92428 (last visited Oct. 19, 2023)

[11] Acyclovir is "a synthetic acyclic purine nucleoside with selective antiviral activity; it is active against most known species of human herpesviruses, particularly against types 1 and 2, which cause herpes simplex. It is used in the treatment of genital and mucocutaneous herpesvirus infections; administered orally or topically." Acyclovir, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=833 (last visited Oct. 19, 2023)

[12] VAERS is a "national early warning system to detect possible safety problems in [] vaccines" co-managed by the Centers for Disease Control and Prevention ("CDC") and the U.S. Food and Drug Administration ("FDA"). About VAERS, https://vaers.hhs.gov/about.html (last visited Oct. 19, 2023). "VAERS accepts and analyzes reports of adverse events (possible side effects) after a person has received a vaccination. Anyone can report an adverse event to VAERS. Healthcare professionals are required to report certain adverse events." Id.

[13] Reference to left side drooping appears to be an error, since all other records document drooping of the right eye and right-sided symptoms.

[14] Blisters or vesicles can be seen in Ramsay Hunt syndrome, and acute facial paralysis caused by the herpes zoster virus. See Pet. Ex. 19 at 3.

lack of tears or sensitivity to light." Id. Symptoms started 10 days prior. Id. Petitioner reported "her [Bell's] palsy [was] somewhat improving but she continue[d] to have pain above her right ear [and] right side of face." Id. It was noted that "[p]ossible contributing factors might include [that she] received [f]lu shot at work [two] weeks ago." Id. Neurologic examination showed abnormal fifth and seventh cranial nerve function. Id. at 35. Diagnosis was Bell's palsy. Id. She was prescribed prednisone and tramadol for pain and was instructed to follow-up if there were no improvements of symptoms in two weeks. Id.

At an optometry appointment in December 2017, Petitioner reported a "noticeable decline or change in vision." Pet. Ex. 5 at 4. Notes indicated Petitioner was "[r]eferred to Patti Wieissler for acupuncture for [r]ight side [B]ell's palsy [with] October 2017 onset." Id. at 5.

On March 28, 2018, Petitioner followed up with her PCP. Pet. Ex. 3 at 40. Petitioner reported she was "still having issues from her Bell's palsy which was diagnosed on [October 4, 2017]." Id. Her ongoing symptoms included right eye twitching when she smiled, soreness on the right side of her face, some hearing loss in her right ear, and occasional right eye blurry vision. Id. Petitioner requested a neurology referral for further evaluation. Id. Petitioner also requested a letter for her employer to be exempt from the annual flu vaccine. Id. She stated that "her employer [would] be reporting her adverse reaction to the CDC." Id. at 40, 44. Sonia Villarreal, certified physician's assistant ("PA-C"), wrote,

> [Petitioner] received the [flu] vaccine at her place of employment on [September 21, 2017] then developed symptoms of Bell's [p]alsy on [October 1, 2017]. She was diagnosed with Bell's [p]alsy on [October 4, 2017] when she saw one of our other providers. Please exempt [Petitioner] from any future [flu] vaccines for her employment since she is still dealing with complications since [October 2017].

Id. at 44.

Petitioner presented "with an eight month history of Bell's palsy" to neurologist Dr. Peter Tarbox for a neurological consultation on June 18, 2018. Pet. Ex. 7 at 1. History indicated that "last year she received the flu vaccination and about a week after she developed right ear pain and then numbness to the right tongue and then facial paralysis of the right side." Id. She had "numbness and tingling to the face and some dryness of her vision. She ha[d] decreased field loss to the right." Id. Petitioner reported she had "some recovery with some kinesis noted." Id. It was also noted she had "no significant lower [seventh] nerve recovery resulting with flattening of the smile." Id. Neurological examination showed "right peripheral VII [cranial nerve] weakness on the right." Id. at 3. "She [was] able to close her eyes but [did] have orbicularis oculi eye weakness. She [was] [] able to elevate the right eyebrow. Her orbicularis oris appear[ed] to be weak. She ha[d] some decreased sensitivity to touch subjectively in the right VII [and eight cranial nerve regions]." Id. The remaining cranial nerves were intact. Id. Dr. Tarbox's impression was Bell's palsy and polyneuropathy. Id. at 3-4.[15] He recommended

[15] On neurological examination, Dr. Tarbox also noted decreased sensitivity in the distribution of the eighth cranial nerve. Pet. Ex. 7 at 3.

electrical stimulation, massages, and acupuncture. Id. at 4. Dr. Tarbox advised Petitioner that given she was "eight to nine months [into] recovery there may be minimal significant recovery from [her current] state," but that nerve recovery was still possible for up to 18-months. Id.

On August 13, 2018, Petitioner followed up with Dr. Tarbox. Pet. Ex. 7 at 18. She reported "no Bell's palsy flare ups" since her last visit but continued to have "numbness and tingling on [her] right side with a mild facial droop." Id. Dr. Tarbox recommended Bell's palsy specific physical therapy. Id. at 20. Petitioner completed three sessions of physical therapy from August 28 to September 11, 2018 with Amapola Mallari, physical therapist ("PT"). See Pet. Ex. 8 at 1-8.

Petitioner returned to her PCP on September 27, 2018. Pet. Ex. 3 at 45. She was still experiencing a "drooping right eye, inability to smile, and pain in [her] right ear. Id. A neurological examination showed abnormal fifth and seventh cranial nerve function. Id. at 46. Petitioner requested a referral to an ear, nose, and throat ("ENT") specialist. Id. at 47.

On September 28, 2018, Petitioner presented to ENT Dr. Walter Bain. Pet. Ex. 6 at 1. History indicated she had hearing loss, taste decrease, and vertigo due to Bell's palsy on October 3, 2017. Id. Examination showed a 50% reduction in strength on the right side of her face, cerumen impaction, and mild bilateral sensorineural hearing loss with audiology measurements in the normal range. Id. at 2-4.[16]

Petitioner had a speech evaluation on January 29, 2019. Pet. Ex. 40 at 1. She described difficulty eating and drinking as well as pain when she moved the right side of her face. Id. After reviewing her history and prior testing, the speech therapist ultimately determined that "no speech therapy [was] recommended at [that] time" due to "very poor rehabilitative potential." Id. at 3.

On March 5, 2019, Petitioner presented Dr. Jackson, another ENT, for complaints of dizziness, hearing loss and ear pain, pain swallowing, difficulty with speech, and facial weakness. Pet. Ex. 38 at 1-3. History indicated Petitioner "developed weakness in the right side of her face" in October 2017. Id. at 1. "She denied having evidence of shingles or other symptoms when the facial weakness occurred, although she had undergone a flu shot [two] weeks earlier." Id. "She reported that her facial function improved about 50% over the ensuing [three] months, but she was left with residual facial weakness." Id. Dr. Jackson summarized Petitioner's onset of symptoms:

> With the onset of facial weakness, she also noticed symptoms including right eye/mouth dryness, right aural fullness, right tinnitus, and imbalance. She reported right sided constant aural fullness. At onset of facial weakness, she noticed temporary right sided hearing loss. She also [] noted that her right sided hearing [] decreased when the aural fullness [was] severe. She reported

[16] The audiogram showed mild relative elevation thresholds but were largely within normal limits. Pet. Ex. 38 at 1.

> intermittent dizziness described as imbalance. She reported that her dizziness [] occurred more in the morning and late afternoon. She reported her imbalance to be mild severity, although it [] fluctuated in severity and [] worsen[ed] when her right aural fullness [was] most pronounced. She reported right sided intermittent tinnitus described as humming. She reported that the tinnitus [] occurred 1-2 times daily and [] lasted for seconds at a time. She reported right sided pain below her right ear which radiate[d] to her jaw.

Id. He also noted Petitioner "reported allergy symptoms described as nasal congestion, nasal discharge, postnasal drip, and eye dryness." Id.

Petitioner's examination by Dr. Jackson, including audiogram and tympanograms, was normal. Pet. Ex. 38 at 2-5. House-Brackman[17] grade was noted to be "II-III/VI" on the right side. Id. at 4. Petitioner had another MRI which was normal. Id. at 8. The treatment plan included further testing to find the cause of the dizziness and hearing symptoms. Id. at 5-6. Facial physical therapy was also recommended. Id. at 5.

On October 2, 2019, Petitioner had an initial physical therapy examination with Diana Schonoff, doctor of PT ("DPT"), at Garden Ridge Physical Therapy & Wellness Center. Pet. Ex. 45 at 1. It was noted that Petitioner got the flu vaccine on September 21, 2017, then two weeks later, on October 1, 2017, developed "pain posterior [right] ear to jaw . . . then facial paralysis [right] side." Id. at 2. Petitioner reported she "did not go to [physical therapy] [] as recommended but [she was] ready now." Id. Petitioner's chief complaints included pain, swelling, and numbness in her right facial, ear, and neck region as well as issues with eating and swallowing. Id. She reported feeling "self conscious eating or talking in front of people due to synkinesis eye closure with mouth movements." Id. House-Brackman was a grade III. Id. Dr. Schonoff recommended physical therapy two to three times per week for a total of 18 sessions. Id. at 3-4.

On October 23, 2020, Petitioner had a telehealth visit with Dr. Maria Alvarez of Neurology Associates. Pet. Ex. 56 at 1. Petitioner reported she had Bell's palsy since 2017. Id. She reported an involuntary right face twitch that was "worse when she [was] tired" and a "heaviness of [her] right face." Id. Petitioner reported the involuntary twitch affected her speech but did not cause any slurring or choking. Id. Dr. Alvarez noted "normal visual fields . . . mild side face weakness, tongue motion normal, no slurring, no focal weakness, [and] no ataxia"[18]

[17] The House-Brackmann facial nerve grading system is the most widely applied scoring system "available to clinically assess the severity of peripheral facial nerve palsy." Pet. Ex. 19 at 2. The House-Brackman grading scale goes from Grade 1 (normal) to Grade 6 (total paralysis). Id. at 3 tbl.b.

[18] Ataxia is "failure of muscular coordination; irregularity of muscular action." Ataxia, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=4630 (last visited Oct. 19, 2023).

during Petitioner's neurological examination. Id. at 2. The use of Botox injections and possible gamma knife surgery was discussed. Id.[19]

Petitioner began Botox treatment in December 2020 and continued through March 2022. Pet. Ex. 59 at 1, 3; Pet. Ex. 61 at 1, 3-4; Pet. Ex. 62 at 1-2, 5; Pet. Ex. 64 at 2. Petitioner reported her facial spams were "stable" and getting "better with therapy." Pet. Ex. 62 at 1; see also Pet. Ex. 61 at 1.

On April 21, 2022, Petitioner had a yearly physical with Diana Lopez, advanced practice registered nurse ("APRN"). Pet. Ex. 65 at 1. Nurse Lopez noted "cranial nerve [V] deficit" during her neurological examination. Id.

No other relevant medical records were submitted.

D. Petitioner's Declaration and Hearing Testimony

On May 25, 2020, Petitioner executed a declaration in response to comments in Respondent's expert's reports questioning whether she had Ramsay Hunt syndrome. Pet. Ex. 46. Throughout, she maintained her diagnosis was Bell's palsy. Id. at 1-2.[20]

At the hearing, Petitioner testified she had been a nurse at Baptist Medical Center for 15 years prior to the flu vaccination at issue. Tr. 7-11. She recalled that prior to September 2017, she was in good health. Tr. 12. She did not have any face, eye, or lip issues prior to the flu vaccine besides needing reading glasses. Tr. 16.

Petitioner discussed the VAERS report submitted on her behalf by her employer. Tr. 12-14. She testified the report stated that she had facial drooping on the left side, which was inaccurate; instead, she had right-side facial drooping. Id. Additionally, Petitioner testified that the employee health nurse advised her that she "should not get the flu vaccine since [she] got Bell's palsy after receiving the flu vaccine" and recommended she obtain an exemption letter from her doctor. Tr. 24; see Pet. Ex. 3 at 44.

About two weeks after receiving her vaccination, Petitioner developed "a really sharp pain behind [her] [right] ear" which was unusual. Tr. 14. She testified it was "really painful," and "something new to [her]" as it had never happened before. Tr. 15. She "had never been seen by a physician for ear problems." Id. On October 2, 2017, Petitioner went to work, because she took some pain medicine and "the pain had subsided." Id. When she got to work, she felt "a little weird, tingling, [and] numbness . . . to the right side of [her] tongue." Id. On October 3,

[19] Botox was also recommended by plastic surgeon, Dr. Agustin Cornejo, in a March 2019 consultation to treat the asymmetry. Pet. Ex. 39 at 3.

[20] Because the parties stipulated that Petitioner was properly diagnosed with Bell's palsy, the undersigned will not discuss this declaration further as it only pertains to the Ramsay Hunt versus Bell's palsy issue. See Joint Prehearing Submission at 1; Pet. Ex. 46.

Petitioner was off from work and when she woke up that morning, she noticed a drooping of her face. Id. She was unable to brush her teeth without difficulty. Id. Her eye was also affected. Id. Her face was paralyzed, "like frozen," and she was unable to close her eye. Id.

Because Petitioner had seen Bell's palsy before in the scope of her work as a nurse, she thought she was having either Bell's palsy or a stroke. Tr. 20. Accordingly, Petitioner recalled that when she started experiencing these symptoms, she sought treatment from her PCP. Id. She went to her PCP "the day after getting Bell's palsy, so it was October 4, 2017." Id. Petitioner testified that the doctor asked her if she had blisters or herpes or any sores anywhere on her body or facial area which Petitioner responded "no."[21] Tr. 22. Petitioner was given medication and steroids. Id.

Petitioner recalled that she returned to her PCP on October 11, 2017 because her condition was worsening. Tr. 22. She was having "a lot of dryness to [her] eye, dryness to [her] mouth, . . . a lot of pain, [and] a lot of spasms, like charley horses [in] back of [her] ear to the jaw area, pulling of [her] neck." Id. She had problems eating and drinking, drooling, and sensitivity of her ear and right side. Tr. 22-23. Because she was not able to close her eye, it was dry and irritated. Tr. 23. She developed blurred vision and used lubricating ointment and eyedrops. Id. Petitioner wore an eye mask at night to sleep and when she showered, she put a towel band over her eye to prevent soap from getting into her eye. Tr. 24.

In her testimony, Petitioner stated that her final diagnosis was Bell's palsy. Tr. 23. She testified that her treating physicians "did not see any blisters, any sores" and so they believed the cause was "possibl[y] [the] flu vaccine." Id. She saw a neurologist in June 2018 due to continued symptoms. Tr. 25. Recommended treatment included physical therapy, Botox, and acupuncture. Tr. 25-26. Petitioner underwent all of the recommended treatment. Id. Petitioner also described the photographs filed showing the effect of Bell's palsy on her facial appearance. Tr. 17-19.

As of the date of the hearing, October 18, 2022, Petitioner was still experiencing "synkinesis, [] blurriness, and vision problems." Tr. 26. She was still unable to completely close her eye and had continued dryness of her eye and mouth. Id. She also had difficulty chewing food and had spasms of the right side of her face. Id.

E. Expert Reports

1. Petitioner's Expert, Dr. Lawrence Steinman[22]

[21] Petitioner testified that despite the records indicating such, she was not asked about a prior history of chickenpox. Tr. 21; see Pet. Ex. 3 at 27. If she had been asked, Petitioner would have answered that she did have chicken pox when she was between the age of seven and eight years old. Tr. 21.

[22] Dr. Steinman submitted four expert reports in this matter and testified at the entitlement hearing. Pet. Exs. 10, 47, 75, 83; Tr. 3, 145.

a. Background and Qualifications

Dr. Steinman is board certified in neurology and has practiced neurology at Stanford University for over 40 years. Pet. Ex. 10 at 1; Pet. Ex. 11 at 2. He received his B.A. from Dartmouth College in 1968 and his M.D. from Harvard University in 1973. Pet. Ex. 11 at 1. Thereafter, he completed an internship in surgery, a residency in pediatrics, and a residency in pediatric and adult neurology from Stanford University Hospital, as well as three fellowships. Id. He currently works as a Professor at Stanford University. Id. Dr. Steinman is also "actively involved in patient care" and has cared for hundreds of adults and children with various neuroinflammatory diseases, including Bell's palsy, transverse myelitis, Guillain-Barré syndrome ("GBS"),[23] acute disseminated encephalomyelitis, neuromyelitis optica, and multiple sclerosis. Pet. Ex. 10 at 1; see also Tr. 59. He has authored or co-authored over 500 publications. Pet. Ex. 11 at 5-47.

b. Opinion

Dr. Steinman opined "to a high degree of medical certainty and by a preponderance of evidence," the contents of the flu vaccine Petitioner received on September 21, 2017, through the mechanism of molecular mimicry, triggered Petitioner's Bell's palsy ten days post-vaccination. Pet. Ex. 10 at 1; see also Tr. 61. He offered several mimics to explain how the flu vaccine can trigger an immune cross-reaction and cause Bell's palsy. Pet. Ex. 10 at 17.

i. Althen Prong One

The mechanistic theory proposed by Dr. Steinman for how the flu vaccine can cause Bell's palsy was molecular mimicry. Pet. Ex. 10 at 6. He explained, molecular mimicry is the concept whereby "shared structures on a virus or bacteria or in a vaccine can trigger a cross-reactive response to self[-antigens]." Id. (citing Pet. Ex. 24 at 3).[24] "In some people, . . . a foreign antigen may resemble antigen produced by the body. Such molecular mimicry provokes the T cells to attack the body tissues that contain the self-antigens." Pet. Ex. 24 at 3.

In support of his theory generally, Dr. Steinman first described Bell's palsy and compared it with GBS. Tr. 63-64. Dr. Steinman described Bell's palsy as "an inflammatory disease of the facial nerve" and like GBS, is an "acute demyelinating disease of the peripheral nervous system." Tr. 61; Pet. Ex. 19 at 4. "In most cases, Bell's palsy is a mononeuritic variant

[23] GBS is a "rapidly progressive ascending motor neuron paralysis of unknown etiology, frequently seen after an enteric or respiratory infection. An autoimmune mechanism following viral infection has been postulated." Guillain-Barré Syndrome, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=110689 (last visited Oct. 19, 2023); see also Pet. Ex. 19 at 1 (describing GBS as a neurologic disorder with a recognized "cell-mediated immunity against peripheral nerve myelin antigens").

[24] Lawrence Steinman, Autoimmune Disease, 269 Sci. Am. 107 (1993).

of [GBS]." Pet. Ex. 19 at 4; see also Tr. 63-64 (testifying there is strong evidence suggesting Bell's palsy is a manifestation of a peripheral neuropathy). While Dr. Steinman acknowledged the cause of Bell's palsy remains unknown, viral infections or an autoimmune process have been postulated. Pet. Ex. 10 at 5 (citing Pet. Ex. 19 at 1). Greco et al. explained that Bell's palsy and GBS may share a similar etiology and pathogenesis, which includes an "autoimmunity cell-mediated reaction against a protein of the peripheral nerve myelin." Pet. Ex. 19 at 1, 5; see also Pet. Ex. 53 at 1 (providing a general overview of three potential mechanisms for viral induced autoimmune diseases: molecular mimicry, bystander activation and persistent virus infection).[25] Accordingly, Dr. Steinman intermittently referred to GBS literature in support of molecular mimicry.

Dr. Steinman proposed two separate and independent "pillars" or theories to illustrate how molecular mimicry could trigger Bell's palsy following flu vaccination. Pet. Ex. 10 at 7; Tr. 64-65. He described how the contents of the flu vaccine "share structural similarities with the proteins glycolipids in the facial nerve including gangliosides and the P2 protein." Pet. Ex. 10 at 6, 16.[26] Thus, his two theories are based on homology between components of the flu vaccine with (1) gangliosides in the peripheral nerve myelin and (2) with P2 protein of the peripheral myelin.

1. Ganglioside Theory

Dr. Steinman's first proposed theory is that the Flucelvax[27] vaccine "likely triggered an anti-ganglioside immune response leading to Bell's [p]alsy, due to the presence of an H1N1 component." Pet. Ex. 10 at 7 (emphasis omitted).

At the hearing, Dr. Steinman opined that gangliosides are recognized as a component in the flu vaccine that could trigger GBS. Tr. 67. In support of this opinion, he cited the Institute of Medicine's ("IOM")[28] acknowledgment that "the ganglioside molecular mimicry theory" is "the premier example of how something in a vaccine could cause . . . [GBS]." Id. (citing Pet. Ex.

[25] Robert S. Fujinami et al., Molecular Mimicry, Bystander Activation, or Viral Persistence: Infections and Autoimmune Disease, 19 Clinical Microbiology Revs. 80 (2006).

[26] According to Dr. Steinman, the peripheral nerve protein, P1L, is now known as P2 peripheral myelin protein. Pet. Ex. 10 at 6; Tr. 231-33.

[27] The flu vaccine Petitioner received was the 2017-2018 Flucelvax. Pet. Ex. 1 at 1; see Pet. Ex. 84 (package insert).

[28] Inst. of Med., Evaluating Biological Mechanisms of Adverse Events, in Adverse Effects of Vaccines: Evidence and Causality 57 (Kathleen Stratton et al. eds., 2012). The IOM is now the National Academy of Medicine.

18 at 99-101). He noted Ang et al.[29] published one of the first papers asserting that molecular mimicry plays a role in inflammatory neuropathy. Pet. Ex. 10 at 7 (citing Pet. Ex. 25). They showed that a ganglioside antibody from the bacteria *Campylobacter jejuni* ("*C. jejuni*")[30] was detected in GBS. Id. (citing Pet. Ex. 25 at 1). The ganglioside antibody was also found in patients with Miller Fisher syndrome[31] "where the facial nerve is often targeted." Id. (citing Pet. Ex. 25 at 1).

Dr. Steinman explained that while gangliosides are not proteins (they consists of sugar and lipid components), "they bind to proteins and they glycosylate[32] proteins in the nervous system." Tr. 208. As such, gangliosides are myelin carbohydrates. Pet. Ex. 10 at 7. Ang et al. concluded that "molecular mimicry between *C. jejuni* [lipopolysaccharides] and gangliosides plays a key role in the induction of antiganglioside antibodies and neurological symptoms in patients with GBS and [Miller Fisher syndrome]." Pet. Ex. 25 at 6; see also Pet. Ex. 27 at 1

[29] C.W. Ang et al., Structure of *Campylobacter jejuni* Lipopolysaccharides Determines Antiganglioside Specificity and Clinical Features of Guillain-Barré and Miller Fisher Patients, 70 Infection & Immunity 1202 (2002).

[30] Dr. Steinman testified that *C. jejuni* is a "gastrointestinal bacteria known to be associated with [GBS], and like many bacteria, it has ganglioside, and we have in our nervous system ganglioside." Tr. 66.

[31] Miller Fisher syndrome is "a variant of [GBS] characterized by areflexia, ataxia, and ophthalmoplegia." Fisher Syndrome, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=110608 (last visited Oct. 19, 2023). Areflexia is the "absence of reflexes." Areflexia, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=4035 (last visited Oct. 19, 2023). Ophthalmoplegia is the "paralysis of the eye muscles." Ophthalmoplegia, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=35269 (last visited Oct. 19, 2023).

[32] Glycosylation is "the formation of linkages with glycosyl groups." Glycosylation, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=20670 (last visited Oct. 23, 2023); see also Tr. 173 (Respondent's expert, Dr. Whitton, testifying that glycosylation "just means adding sugars to").

(indicating that the anti-GQ1b antibodies[33] found in patients with Miller Fisher syndrome and other related conditions may be "due to the different expression of gangliosides in different parts of the nervous system");[34] Pet. Ex. 28 at 2-3 (noting ganglion involvement in isolated cranial neuropathies like Bell's palsy).[35]

Dr. Steinman cited medical articles that examined whether flu vaccines could elicit anti-ganglioside responses in the absence of *C. jejuni*. Nachamkin et al.[36] found that vaccines containing H1N1 induced anti-GM1 antibodies[37] in mice. Pet. Ex. 26 at 1, 5. They also found antibody responses to hemagglutinin; a viral surface glycoprotein found in H1N1. Id. They determined hemagglutinin could bind to cellular gangliosides and mimic an anti-ganglioside antibody using the 1976 swine flu vaccine, which contained H1N1. Id.; see also Tr. 66. While Dr. Steinman acknowledged that Nachamkin et al. did not test the 2017-2018 flu vaccine, he explained that the 2017-2018 flu vaccine contained H1N1 component like the vaccine studied by Nachamkin et al. Pet. Ex. 10 at 7; see Pet. Ex. 23 at 2.[38] Dr. Steinman also cited An et al.,[39] which provided that the manner in which hemagglutinin is glycosylated may impact immune processing leading to molecular mimicry. Pet. Ex. 50 at 1.

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[33] Anti-GQ1b IgG antibodies are immune markers for Miller Fisher syndrome and GBS. See Pet. Ex. 28 at 1. "A common role of serum GQ1b antibodies in the pathogenic mechanism of these conditions have been supported by a study of the ganglioside composition of human cranial nerves that reveal a high concentration of GQ1b epitopes in the paranodal region and Ranvier nodes of the extramedually parts, particularly of the III, IV, and V [cranial] nerves." Id. at 2. Nodes of Ranvier are "constrictions occurring on myelinated nerve fibers at regular intervals of about 1 mm; at these sites the myelin sheath is absent and the axon is enclosed only by Schwann cell processes." Nodes of Ranvier, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=93095 (last visited Oct. 19, 2023).

[34] Y. Fukami et al., Anti-GQ1b Antibody Syndrome: Anti-Ganglioside Complex Reactivity Determines Clinical Spectrum, 23 Eur. J. Neurology 320 (2016).

[35] Filippo Greco et al., Recurrent Facial Nerve Palsy Associated with Anti-GQ1b IgG Antibodies, 30 Brain & Development 606 (2008).

[36] Irving Nachamkin et al., Anti-Ganglioside Antibody Induction by Swine (A/NJ/1976/H1N1) and Other Influenza Vaccines: Insights into Vaccine-Associated Guillain-Barré Syndrome, 198 J. Infectious Diseases 226 (2008).

[37] Ganglioside GM-1 is "one of several gangliosides considered a target antigen in the pathogenesis of GBS." Pet. Ex. 26 at 5.

[38] U.S. Food & Drug Admin., Influenza Virus Vaccine for the 2017-2018 Season, (last updated Nov. 30, 2017).

[39] Yanming An et al., N-Glycosylation of Seasonal Influenza Vaccine Hemagglutinins: Implication for Potency Testing and Immune Processing, 93 J. Virology e01693 (2019).

The vaccines studied by Nachamkin et al. were egg-based. Tr. 66; Pet. Ex. 26 at 2. Dr. Steinman testified that the research showed "in the rich environment of an egg growing [flu] virus, that the [flu] proteins, like the hemagglutinin and neuraminidase, get glycosylated." Tr. 88. Dr. Steinman explained that the 2017-2018 Flucelvax vaccine was not egg-based but instead grown from canine kidney cells. Tr. 66-67; Pet. Ex. 84 at 10. Dr. Steinman testified that "canine kidney cells are very good at glycosylating. Tr. 67. Thus, Dr. Steinman opined that an egg-based vaccine was not required for molecular mimicry. Id. Likewise, he opined that *C. jejuni* was not needed. Id. In fact, he believed that canine kidney cells are "even better than the egg cultures at glycosylating the [flu] proteins." Tr. 86-87.[40] Dr. Steinman concluded that "[a] ganglioside is a ganglioside whether the chemistry is in a chicken egg or a canine kidney cell or a human cell." Pet. Ex. 47 at 4; see also Tr. 89 ("A ganglioside from a dog is the same as a ganglioside from a chicken.").

Accordingly, Dr. Steinman opined that a human getting a flu vaccine can "mount a response to ganglioside" and that "anti-ganglioside antibodies are associated with facial nerve palsy." Tr. 210-11; Pet. Ex. 10 at 7 (citing Pet. Exs. 19, 27);[41] see also Pet. Ex. 18 at 101.

2. P2 Protein Theory

The second theory proposed by Dr. Steinman is that there is molecular mimicry between components of the flu vaccine and the P2 protein in myelin. Pet. Ex. 10 at 7. Dr. Steinman opined that "P2 is attacked in Bell's palsy." Tr. 56.

Dr. Steinman cited Abramsky et al.[42] to show that "[i]mmune responses to P2 have been associated with Bell's [p]alsy [] and inflammatory neuropathy" thus supporting a cell-mediated autoimmune mechanism in Bell's palsy. Pet. Ex. 10 at 6-7 (citing Pet. Ex. 20 at 1, 4 fig.1). Abramsky et al. "demonstrated a defined in vitro response to a human basic protein [] of peripheral nerve myelin in patients with Bell's palsy" resulting in immunologic lymphocyte alterations. Pet. Ex. 20 at 5. This response suggests that the sensitization of lymphocytes to the self-protein "may be an important factor in the pathogenesis of the paralysis." Id. at 7.

The human basic protein in peripheral nerve protein discussed in Abramsky et al. was referred to as the P1L protein. See Pet. Ex. 20 at 5. According to Dr. Steinman, the P1L protein described in Abramsky et al. is now known as the P2 peripheral myelin protein. Pet. Ex. 10 at 6; Tr. 231-33. To explain this change, Dr. Steinman cited a paper he co-authored that was

[40] For more discussion on the foundation for this opinion, see Tr. 87-88; Pet. Ex. 47 at 4; Pet. Ex. 50 at 10, 12 tbl.3; Pet. Ex. 49 at 1.

[41] Y. Fukami et al., Anti-GQ1b Antibody Syndrome: Anti-Ganglioside Complex Reactivity Determines Clinical Spectrum, 23 Eur. J. Neurology 320 (2016).

[42] O. Abramsky et al., Cellular Immune Response to Peripheral Nerve Basic Protein in Idiopathic Facial Paralysis (Bell's Palsy), 26 J. Neurological Sci. 13 (1975).

published in 1981. Tr. 57-58; Pet. Ex. 22 at 1.[43] In the study, Dr. Steinman and colleagues immunized rats of different genetic backgrounds with the P2 protein to show that the P2 protein can cross paths with the flu vaccine to cause cranial nerve damages. Tr. 58; Pet. Ex. 22 at 1. Their findings can be summarized as follows:

> Experimental allergic neuritis (EAN) is an inflammatory demyelinating peripheral neuropathy induced by immunization against components of peripheral nervous system [] myelin. EAN appears after immunization of the Lewis rat with purified [peripheral nervous system] myelin from many other species. Myelin of the [peripheral nervous system] contains two major basic proteins: P1 protein (molecular weight, 18,000) is similar or identical to central nervous system (CNS) myelin basic protein, the encephalitogen responsible for experimental allergic encephalomyelitis (EAE). A smaller basic protein, P2 (molecular weight, 12,000), has an amino acid composition unrelated to P1. The critical antigen responsible for the induction of EAN is P2.

Pet. Ex. 22 at 1.

Accordingly, Dr. Steinman explained that the change of nomenclature from P1 to P2 is based on molecular weights of the proteins and one of the proteins, P1L, is not in the peripheral nervous system. Tr. 236. Further, the authors of the 1981 paper found that the critical antigen responsible for induction of EAN was the P2 protein. Id.; Pet. Ex. 22 at 1; see also Pet. Ex. 86 at 1 (suggesting the P2 protein is the antigen responsible for EAN).[44]

Following the hearing, Dr. Steinman submitted a supplemental report and literature to further clarify the nomenclature issue of P1L protein and P2 protein. See Pet. Exs. 83-88. He explained the "species of the P2 is [] important in assigning what molecular weight the P2 protein has, since the P2 proteins are of varying lengths and amino acid composition from species to species." Pet. Ex. 83 at 3. Citing Kadlubowski and Hughes,[45] Dr. Steinman wrote that P1 refers to myelin basic protein with a molecular weight of 18,000, and P2 refers to myelin basic protein with molecular weights of 12,000-14,000, "depending on the species." Id. (citing Pet. Ex. 88 at 1).

According to Dr. Steinman, Kadlubowski and Hughes "report[ed] the 'issues' surrounding P1L[] that led to its renaming of P2." Pet. Ex. 83 at 3. They wrote, "[o]f the two

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[43] Lawrence Steinman et al., Genetic Control of Susceptibility to Experimental Allergic Neuritis and the Immune Response to P2 Protein, 31 Neurology 950 (1981).

[44] S.W. Brostoff & E.H. Eylar, The Proposed Amino Acid Sequence of the P1 Protein of Rabbit Sciatic Nerve Myelin, 153 Archives Biochemistry & Biophysics 590 (1972).

[45] M. Kadlubowski & R.A.C. Hughes, Identification of the Neuritogen for Experimental Allergic Neuritis, 277 Nature 140 (1979).

basic proteins in peripheral myelin, P1 has been shown to be the same as the encephalitogenic[46] basic protein in the rabbit sciatic nerve, and this is likely to be the same for other species." Pet. Ex. 88 at 2; see also Pet. Ex. 86 at 1. "Thus, attention has focused on the other basic protein, P2, which may be specific to peripheral nerve myelin." Pet. Ex. 88 at 2. All were ultimately unsuccessful, suggesting that "isolation might lead to an alteration in the considerable secondary structure of P2." Id. Additional papers explored the P2 protein,[47] and ultimately were "able to isolate P2 in a form which is neuritogenic." Id. Brostoff et al.[48] also studied P2 as the myelin basic proteins in the peripheral nervous system. Pet. Ex. 87 at 1. "Another, smaller basic protein ([molecular weight] 12,000) is almost always present as well in [peripheral nervous system] myelin. This smaller protein, referred to as the P2 protein, seems to be a unique [peripheral nervous system] protein with no relationship to the larger basic protein." Id. (internal citations omitted).[49] After a review of the relevant studies and findings, Dr. Steinman concluded that "P1L, the neuritogenic protein that triggered Bell's palsy" in Abramsky et al. was renamed to P2. Pet. Ex. 83 at 4.

After verifying "that P2 is targeted in Bell's palsy," Dr. Steinman used a three-step process to identify protein sequences that could implicate molecular mimicry between the flu vaccine and the P2 antigen. Tr. 69; see Tr. 212, 215; Pet. Ex. 47 at 7-8. First, Dr. Steinman conducted a BLAST[50] search to determine whether there was any similarity, or sequence homology, between the components of the 2017-2018 Flucelvax vaccine and the myelin protein P2. Tr. 69; see also Pet. Ex. 10 at 7, 10.[51] Dr. Steinman started by looking at one of the proteins

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[46] Dr. Steinman opined encephalitogenic means "it is in the brain." Pet. Ex. 83 at 4.

[47] S.W. Brostoff et al., Induction of Experimental Allergic Neuritis with a Peptide from Myelin P2 Basic Protein, 268 Nature 752 (1977). This article was not filed.

[48] S.W. Brostoff et al., The P2 Protein of Bovine Root Myelin: Partial Chemical Characterization, 24 J. Neurochemistry 289 (1975).

[49] For additional discussion of the P1L and P2L issue, see Pet. Ex. 83 at 3-4; Tr. 237; Pet. Ex. 20 at 3.

[50] A BLAST (Basic Local Alignment Search Tool) search "finds regions of similarity between biological sequences. The program compares nucleotide or protein sequences to sequence databases and calculates the statistical significance." BLAST, https://blast.ncbi.nlm.nih.gov/Blast.cgi (last visited Sept. 8, 2023). Dr. Steinman testified that this cannot be done with regard to his ganglioside theory because a "BLAST search is suitable for seeing the similarity between one protein and another," not for a sugar. Tr. 68.

[51] For a complete explanation of Dr. Steinman's investigation, including his discussion on the number of amino acids required for homology relevant to molecular mimicry as well as the procedure he followed in conducting his BLAST searches, see Pet. Ex. 10 at 7-15; Pet. Ex. 47 at 7-12; Pet. Ex. 75 at 1-4; Tr. 73, 217-18

in the flu vaccine, hemagglutinin. Tr. 73-74; see also Pet. Ex. 23 at 2.[52] He found "a 5 of 11 exact homology[53] in amino acids for the P2 protein and a component of hemagglutinin of the [flu] A virus (A/Michigan/45/2015(H1N1)) found in the 2017-2018 [flu] vaccine." Pet. Ex. 10 at 10; see also Tr. 69-70, 73. He also found another component of the vaccine had sequence homology with the P2 protein,[54] and noted that not all components of the 2017-2018 flu vaccine do. Pet. Ex. 10 at 11-12; Tr. 73-74.

Next, Dr. Steinman filtered the areas of alignment between the vaccine and the myelin protein P2 from the BLAST search and "eliminate[d] sequence homologies that [were] below a threshold that ha[d] been shown to induce neuroinflammation with clinical symptoms like paralysis in the [experimental encephalomyelitis ("EAE")] model." Pet. Ex. 47 at 7. Relying on medical literature, Dr. Steinman opined the sequence he found was significant due to the presence of five identical amino acids in a longer sequence. Pet. Ex. 10 at 11; Pet. Ex. 75 at 1-3; Tr. 70. For support, he cited Lanz et al.,[55] which found five out of 12 identical amino acids for molecular mimicry between Epstein-Barr virus and multiple sclerosis. Pet. Ex. 76 at 1; Tr. 216, 218-19.

Additionally, studies by Gautam et al. found "[five] of 12 amino acids, not even consecutive amino acids, was sufficient to trigger [EAE]." Pet. Ex. 10 at 7 (citing Pet. Ex. 29 at

[52] Dr. Steinman testified that hemagglutinin and neuraminidase are the H and N of H1N1. Tr. 74.

[53] The five identical amino acids Dr. Steinman identified were YKLAT, with YVKSTKLRLAT as the sequence for the hemagglutinin component of the vaccine and YMKALGVGLAT as the sequence for the peripheral myelin protein 2. Pet. Ex. 10 at 11.

[54] "Another homology of similar significance is found in the B Brisbane component and the P2 protein, where the sequence LSTQNVIDAEKA has five of 12 identical amino acids." Pet. Ex. 10 at 11-12.

[55] Tobias V. Lanz et al., Clonally Expanded B Cells in Multiple Sclerosis Bind EBV EBNNA1 and GlialCAM, 603 Nature 321 (2022). Dr. Steinman is a named author in this paper.

1;[56] Pet. Ex. 30 at 1;[57] Pet. Ex. 31 at 1);[58] see also Tr. 46-47. Therefore, Dr. Steinman determined the "[five] of 11 identical amino acids between a component of the vaccine and P2 protein . . . [was] very likely sufficient to trigger clinically relevant inflammation in peripheral nerve." Pet. Ex. 10 at 11 (emphasis omitted); see also Pet. Ex. 47 at 6; Tr. 70.

Dr. Steinman disagreed with Respondent's expert, Dr. Whitton, who asserted that much longer sequences (of 80 amino acids) were required for homology based on the paper by Silvanovich et al.[59] Tr. 214-18 (citing Resp. Ex. C, Tab 10); see also Tr. 176. Instead, Dr. Steinman opined that the immune system interacts with shorter sequences of amino acids. See Tr. 214-18. Further, Dr. Steinman explained that Silvanovich et al. pertained to allergic responses not immune system responses, and thus, it was not relevant. Tr. 93-94; Pet. Ex. 10 at 13. Additionally, Dr. Steinman noted that Silvanovich et al. endorsed the use of BLAST searches. Tr. 94.[60]

The third step of his process "retains those peptide sequences identified in the first two steps, only if they have been identified by other investigators using one and/or two other US government databases." Pet. Ex. 47 at 7. Dr. Steinman searched the sequence, YVKSTKLRLAT, which had 5 of 11 identical amino acids between a component of the vaccine and P2 protein in the Immune Epitope DataBase ("IEDB").[61] Pet. Ex. 47 at 9; Tr. 75, 213-15.

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[56] Anand M. Gautam et al., A Viral Peptide with Limited Homology to a Self Peptide Can Induce Clinical Signs of Experimental Autoimmune Encephalomyelitis, 161 J. Immunology 60 (1998). Dr. Steinman is a named author in this paper.

[57] Anand M. Gautam et al., Minimum Structural Requirements for Peptide Presentation by Major Histocompatibility Complex Class II Molecules: Implications in Induction of Autoimmunity, 91 Immunology 767 (1994). Dr. Steinman is a named author in this paper.

[58] Anand M. Gautam et al., A Polyalanine Peptide with Only Five Native Myelin Basic Protein Residues Induces Autoimmune Encephalomyelitis, 176 J. Experimental Med. 605 (1992). Dr. Steinman is a named author in this paper.

[59] Andre Silvanovich et al., The Value of Short Amino Acid Sequence Matches for Prediction of Protein Allergenicity, 90 Toxicological Scis. 252 (2006).

[60] Silvanovich et al. stated that BLAST searches "rank the similarity of a query protein to its corresponding matches and provide a measure of the reliability of the alignment." Resp. Ex. C, Tab 10 at 7.

[61] The IEDB "catalogs experimental data on antibody and T cell epitopes studied in humans, non-human primates, and other animal species in the context of infectious disease, allergy, autoimmunity and transplantation. The IEDB also hosts tools to assist in the prediction and analysis of epitopes." Immune Epitope Database and Analysis Resource, https://www.iedb.org/ (last updated Sept. 3, 2023). The IEDB is a freely available resource funded by the National Institute of Allergy and Infectious Diseases. Id.

The sequence appeared in the IEDB, which Dr. Steinman asserted was evidence that it was an epitope that had been reported in humans. Pet. Ex. 47 at 8-9; see also Tr. 215. The epitope also appeared in Influenza Research Database ("IRD").[62] Pet. Ex. 47 at 7, 9-10. Dr. Steinman testified that because it was reported in the IEDB and IRD, this indicated that "others have looked at that sequence that was identified and . . . studied it." Tr. 75; see also Tr. 214-15. "Other immunologists show that this is actually recognized by the immune system when they're looking at hemagglutinin, [and the] similarity between P2 and the hemagglutinin." Tr. 75; see also Pet. Ex. 47 at 9.

After explaining his two theories, Dr. Steinman acknowledged the limitations to this process of illustrating molecular mimicry and sequence homology. See, e.g., Pet. Ex. 75 at 2, 5-6.[63] However, because he was unable to perform research on the Petitioner, and because there is "no animal model for Bell's palsy," he asserted that his "three steps of filtration using peer reviewed journals . . . three different US government-financed search tools (BLAST, IEDB, and IRD) make a compelling theory that molecular mimics in the [flu] vaccine received by [P]etitioner could trigger immunity to P2 myelin protein." Pet. Ex. 47 at 12 (emphasis omitted); see also Tr. 48. He emphasized that his opinions that there are "homologies with antigens that are homologous mimics of the vaccine and that are targeted in Bell's palsy" are based on Abramsky et al., Winer et al.,[64] Steinman et al., and the criteria from Gautam et al. Pet. Ex. 47 at 12 (citing Pet. Exs. 20-22, 29-31).

Dr. Steinman also opined that "it takes more than a molecular mimic to trigger a disease. [Steinman et al.] says you have to have the right genes." Tr. 58 (citing Pet. Ex. 22 at 5). "Other genetic and environmental factors are necessary before these self-reactive immune responses to myelin might trigger conditions like Bell's palsy." Pet. Ex. 10 at 15-16. Still, he opined molecular mimicry is important in "trying to understand how something can be triggered by a vaccine or by a virus." Tr. 58.

3. Medical Literature and Case Reports

In further support of his opinions, Dr. Steinman cited studies and case reports on the association between the flu vaccine and Bell's palsy. See Pet. Ex. 75 at 6-7. Several of the studies cited by Dr. Steinman acknowledge finding a signal or increased risk of Bell's palsy after administration of the flu vaccination. Id.

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[62] The IRD "is a US NIH/NIAID-funded, freely-available online bioinformatics resource for influenza virus data search, analysis and visualization." Richard H. Scheuermann, Influenza Research Database (IRD), J. Craig Venter Institute, https://www.jcvi.org/research/influenza-research-database-ird (last visited Oct. 23, 2023); see also Bacterial and Viral Bioinformatics Resource Center, https://www.bv-brc.org/ (last visited Oct. 23, 2023).

[63] For the limitations acknowledged by Dr. Steinman, see Tr. 51-52, 74-77.

[64] J.B. Winer et al., A Prospective Study of Acute Idiopathic Neuropathy. I. Clinical Features and Their Prognostic Value, 51 J. Neurology Neurosurgery & Psychiatry 605 (1988).

Zhou et al. reviewed and analyzed VAERS reports between 1991 and 2001 to determine whether there was an association between Bell's palsy and the flu vaccine. Pet. Ex. 73 at 1-2.[65] The authors identified 197 possible cases of Bell's palsy after receipt of a flu vaccine. Id. Of the 197 reports, Bell's palsy diagnosis was verified in 154, and among those, 145 cases received the flu vaccine alone. Id. The authors concluded there "may be a signal of possible association between [flu] vaccines and an increased risk of Bell's palsy." Id. at 5. They noted the etiology and pathogenesis of Bell's palsy is not clear, but that there is "concern that latent [HSV-1] infections of the geniculate ganglia of facial nerves may be one of the causes of Bell's palsy" and that "[i]mmune response mechanisms have also been considered." Id.

Bardage et al.[66] was a population-based study in Sweden with H1N1 vaccine (Pandemrix) from October 2009 and March 2010 which reported an increased risk of Bell's palsy. Pet. Ex. 67 at 2, 4. The authors found "a significantly increased risk for Bell's palsy" in "those vaccinated in the early phase of the vaccination campaign (≤ 45 days), when high risk groups predominated." Id. at 4. "In contrast, among people vaccinated after the first 45 days of the campaign, representing more closely the general population, [they] found no statistically significant associations between vaccination and autoimmune or neurological diseases." Id. The authors concluded that they "[could not] explain the small increase in risk for Bell's palsy seen in this study." Id. at 5.

Next, Dr. Steinman cited a recent 2020 study authored by Kamath et al.[67] who "analyzed [VAERS] data to determine whether the facial paralysis reporting rate is higher in those who received the [flu] vaccination compared with those who received other vaccines." Pet. Ex. 70 at 1. The authors evaluated VAERS reports from January 2015 to October 2019 and identified 250 reports of facial paralysis in patients who received flu vaccines and 346 reports of facial paralysis for all other vaccines. Id. at 3. "[Their] study show[ed] that the likelihood of reporting facial paralysis following [flu] vaccination [was] higher compared with other vaccines." Id. at 4. The authors found an onset median of three (range of 1-10) days but noted "the number of

[65] Zhou et al. also acknowledged the issues and limitations with VAERS, stating, in relevant part, "[d]ata from VAERS should be interpreted with caution because they represent adverse events that occurred after vaccination, not all of which may have been caused by vaccination. Temporal association alone does not mean that the vaccine caused the illness or symptoms." Pet. Ex. 73 at 5.

[66] Carola Bardage et al., Neurological and Autoimmune Disorders After Vaccination Against Pandemic Influenza A (H1N1) with a Monovalent Adjuvanted Vaccine: Population Based Cohort Study in Stockholm, Sweden, 343 BMJ 1 (2011).

[67] Ashwin Kamath et al., Facial Paralysis Following Influenza Vaccination: A Disproportionality Analysis Using the Vaccine Adverse Event Reporting System Database, 20 Clinical Drug Investigation 883 (2020). Like the authors in Zhou et al., the authors acknowledged the limitations in their findings, including the "inherent limitations of the VAERS database analysis and the fact that disproportionality measures only indicate the presence of a signal." Pet. Ex. 70 at 4-6.

patients for whom the time of onset data were recorded was limited." Id. at 5. Most of the cases of facial paralysis occurred within the first two weeks following vaccination with the seasonal trivalent or quadrivalent intramuscular flu vaccine. Id. at 6. They noted "[t]he appearance of Bell's palsy after the vaccination supports the immunological hypothesis." Id. at 4.

Lastly,[68] Dr. Steinman cited Huang et al.,[69] who used a "capture-recapture method to (1) assess the reporting completeness of Taiwan's passive safety surveillance system for selected adverse events after 2009 H1N1 vaccines; and (2) evaluate the risks of these events for the biologically plausible postvaccination risk intervals." Pet. Ex. 69 at 2. The authors identified 1,475 cases of Bell's palsy, with 298 patients developing Bell's palsy 0-42 days after flu vaccination. Id. at 3 tbl.2. The authors also determined the estimated number of Bell's palsy cases that occured 0-42 days after flu vaccination was 525, while the expected number of cases was 354. Id. at 3, 3 tbls.3-4. Huang et al. concluded "[t]here was an increased risk for Bell's palsy in the interval 0-42 days after vaccination." Id. at 3.

In addition to the above studies, Dr. Steinman also cited Chou et al., an article that discussed two case reports of Bell's palsy following flu vaccination. Pet. Ex. 75 at 7 (citing Pet. Ex. 68 at 1). The first was of a 30-year-old male who developed symptoms 10 days after administration of a flu vaccine. Pet. Ex. 68 at 1. He had received a flu vaccine in the past and had no history of any adverse drug reactions, no personal or family history of neurological disorders, and no history of recent infections. Id. The authors found "no other explanation for the Bell's palsy except for the [flu] vaccine. Furthermore, because the peripheral facial palsy presented within [one] month between the vaccination and the onset of neurological symptoms, a causal relationship was suspected . . . when there was no evidence of infection." Id. at 2. The second case report was of an 80-year-old man who developed symptoms three days after flu vaccination. Id. He had a history of type II diabetes and hypertension. Id. He had also received a flu vaccine previously and gave no history of an adverse drug reaction, had no personal or family history of neurological disorders, and no history of recent infections. Id. Because of his history of diabetes and hypertension, the authors were unable to "definitively implicate the [flu] vaccine as etiologic for Bell's palsy." Id.

In response to Respondent's experts' reliance on different epidemiological studies, Dr. Steinman made several observations. He noted that some of the studies do not account for differences in the seasonal flu vaccine from year to year, and therefore, they may not be relevant to the 2017-2018 flu vaccine. Tr. 85, 101. He testified that the cases cited above by Bardage et

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[68] Dr. Steinman also cited an article by Rath et al., regarding the "need to define Bell's palsy as an adverse event following immunization," noting the need to achieve consensus on the definition of the illness and the need to have complete diagnostic testing to assess it as an adverse event. Pet. Ex. 72 at 3 (Barbara Rath et al., "All That Palsies is Not Bell's [1]"—The Need to Define Bell's Palsy As an Adverse Event Following Immunization, 26 Vaccine 1 (2007)).

[69] Wan-Ting Huang et al., The Reporting Completeness of a Passive Safety Surveillance System for Pandemic (H1N1) 2009 Vaccines: A Capture-Recapture Analysis, 30 Vaccine 2168 (2012).

al., Chou et al., and Huang et al. are relevant to the 2017-2018 flu vaccine at issue here because they all contain an H1N1 strain. Tr. 101. Further, he testified that "epidemiology does not rule out the rare case." Tr. 85-86.

ii. Althen Prongs Two and Three

Dr. Steinman opined "the [flu] vaccination that [P]etitioner received on Sept[ember] 21, 2017 contained components that ha[d] chemical structures that [were] cross-reactive with myelin antigens, both the P2 protein and gangliosides. These cross-reactive immune responses triggered Bell's [p]alsy" "ten days later on Oct[ober] 4, 2017." Pet. Ex. 10 at 16-17.

Petitioner received the Flucelvax vaccine on September 21, 2017. Pet. Ex. 10 at 4 (citing Pet. Ex. 1 at 1; Pet. Ex. 2 at 3). Ten days later, on October 4, 2017, Petitioner presented to the South Alamo Medical Group "for evaluation of possible Bell's palsy with drooping right eye and pain in ear. Associated symptoms include[d] difficulty closing eye, drooping lower eyelid, facial muscle weakness[,] and pain near the ear. Symptoms started approximately [three] days before this visit." Id. at 4, 16 (quoting Pet. Ex. 3 at 27). In review of the medical history, Dr. Steinman noted that when Petitioner presented on October 11, 2017, there were "no blisters in or near the ear." Id. at 4 (quoting Pet. Ex. 3 at 33).

The correct diagnosis, in Dr. Steinman's opinion, is Bell's palsy, "the diagnosis made by treating physicians." Pet. Ex. 10 at 4. While he initially noted that alternative causes such as infectious diseases "were ruled out by the treating physicians" because "[n]o anti-viral therapy was given, indicating to [Dr. Steinman] that the treating doctors did not think this was a viral mediated seventh nerve palsy like Ramsay Hunt syndrome," Dr. Steinman later corrected this position. Id.; see also Pet. Ex. 47 at 1; Tr. 99. He acknowledged that antiviral medication was given to Petitioner but that it did not change his opinion or theories that the flu vaccine triggered her Bell's palsy through an immune response. Pet. Ex. 47 at 1; Tr. 99-100.

Moreover, Dr. Steinman noted that the medical records "made the link between the vaccine and [Petitioner's] Bell's [p]alsy as well." Pet. Ex. 10 at 16; see also Pet. Ex. 47 at 13; Pet. Ex. 75 at 8. "It was noted that the possible contributing factor might include the receipt of the flu vaccine two weeks ago." Pet. Ex. 10 at 16 (citing Pet. Ex. 3 at 33). He also pointed out that "a letter was written to exempt [Petitioner] from future [flu] vaccines since she was still dealing with complications since October 2017." Id. (citing Pet. Ex. 3 at 44).

Relying on Schonberger et al.[70] "as a surrogate for how soon a[] [flu] vaccine could trigger clinically relevant inflammation in the peripheral nervous system," Dr. Steinman opined "the timing in this case fits well with the findings from the CDC." Pet. Ex. 10 at 16 (citing Pet. Ex. 36); see also Tr. 83. Schonberger et al. reviewed case reports from the CDC of GBS after the flu vaccine administration and found, on average, an onset between two and three weeks.

[70] Lawrence B. Schonberger et al., Guillain Barré Syndrome Following Vaccination in the National Influenza Immunization Program, United States, 1976-1977, 110 Am J. Epidemiology 105 (1979).

Pet. Ex. 36 at 2. Accordingly, Dr. Steinman opined that 10 days "is absolutely consistent with what could occur between a [flu] vaccine and the onset of an inflammatory neuropathy." Tr. 83.

Further, Zhou et al. found around 77% of the Bell's palsy reports had an onset between one and 30 days after flu vaccination. Pet. Ex. 73 at 4.[71] Kamath et al. similarly found a median range onset of one to 10 days. Pet. Ex. 70 at 5. Huang et al. identified 298 patients who developed Bell's palsy 0-42 days after flu vaccination. Pet. Ex. 69 at 3 tbl.2. And Chou et al. discussed two case reports of Bell's palsy after flu vaccination and reported onset intervals of three days and 10 days. Pet. Ex. 68 at 1-2.

2. Respondent's Expert, Dr. Brian C. Callaghan[72]

a. Background and Qualifications

Dr. Callaghan is an Associate Professor of Neurology at the University of Michigan and "a neuromuscular specialist with a primary interest in patients with neuropathy such as Bell's palsy." Resp. Ex. A at 1. Dr. Callaghan is also a staff physician in the Department of Neurology for the Veterans Affairs Ann Arbor Health System. Resp. Ex. B at 2. He earned his M.D. from the University of Pennsylvania Medical Center and his M.S. in Clinical Research Design and Statistical Analysis at the University of Michigan. Id. at 1. He completed his residency in neurology and completed a neuromuscular fellowship. Id. He serves as co-section editor for a neurology journal, peer reviews for several neurology journals, and has over 120 publications with a focus on neuropathy, including the appropriate diagnostic evaluation and treatment. Id. at 4, 10-17; Tr. 111. Dr. Callaghan testified he has seen approximately 30 patients in his career that have presented with clinical presentations of Bell's palsy. Tr. 108.[73]

b. Opinion

Dr. Callaghan opined that Petitioner's flu vaccination "was not the cause of her facial weakness." Resp. Ex. A at 2. He reasoned "the current literature does not support an association between [flu] vaccination and Bell's palsy." Id.; see also Tr. 126.

i. **Althen** Prong One

[71] The authors stated that "reporting bias may explain the short onset intervals observed in [their] study. Therefore, the short onset interval should be interpreted with caution. It may not represent the true onset time due to the differential reporting bias in a passive surveillance system." Pet. Ex. 73 at 5.

[72] Dr. Callaghan submitted two expert reports in this matter and testified at the entitlement hearing. Resp. Exs. A, G; Tr. 3, 145.

[73] Dr. Callaghan testified that Bell's palsy is "a relatively benign condition in that most patients . . . don't always come to neurologists, and they often don't need neuromuscular specialists. But when they're complicated, they do." Tr. 108.

In his first expert report, Dr. Callaghan focused on his opinion that "the current literature does not support an association between [flu] vaccination and Bell's palsy." Resp. Ex. A at 2; see also Tr. 126. Dr. Callaghan opined that "the mechanism of Bell's palsy is not well known and the papers that Dr. Steinman provide[d] [were] based on GBS and MS." Resp. Ex. A at 2. In support of his opinion, Dr. Callaghan cited several works of medical literature that he claimed, "do[] not support an association between [flu] vaccination and Bell's palsy." Id.; see also Tr. 118-19.

First, Dr. Callaghan cited Mutsch et al.,[74] which "investigated the association between the intranasal [flu] vaccination in Switzerland with Bell's palsy and found a strong relationship." Resp. Ex. A at 2 (citing Resp. Ex. A, Tab 1 at 1).[75] However, according to Dr. Callaghan, they "did not find an association with the parenteral [flu] vaccination." Id. (citing Resp. Ex. A, Tab 1 at 6). The authors found that "[i]n contrast to the parenteral vaccines, the intranasal vaccine significantly increased the risk of Bell's palsy" and that "there was essentially no risk of Bell's palsy after receipt of the traditional, parenteral [flu] vaccine." Resp. Ex. A, Tab 1 at 1, 4.

Stowe et al.[76] "investigated the association between the parenteral [flu] vaccination and the pneumococcal vaccination with Bell's palsy." Resp. Ex. A at 2 (citing Resp. Ex. A, Tab 2 at 1).[77] The population-based study of 2,128 individuals who developed Bell's palsy from 1992 to 2005 found "no evidence of an increased risk [of Bell's palsy] in the three months following parenteral inactivated [flu] vaccine." Resp. Ex. A, Tab 2 at 1-2. They also found no increased risk of Bell's palsy following the pneumococcal vaccination. Id. The authors wrote, "[t]his study suggests that the association seen with the inactivated intranasal [flu] vaccine may be specific to the administration of the intranasal vaccine and the association observed cannot be extrapolated to the parenteral inactivated vaccine." Id. at 3.

Rowhani-Rahbar et al.[78] examined the association between Bell's palsy and vaccines in children within the patient data base of Kaiser Permanente Northern California from 2001 to

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[74] Margot Mutsch et al., Use of the Inactivated Intranasal Influenza Vaccine and the Risk of Bell's Palsy in Switzerland, 350 New Eng. J. Med. 896 (2004).

[75] The Mutsch et al. study examined data in Switzerland from 2000 to 2001, and the article does not reference the H1N1 as part of the flu vaccine administered during that time frame. See Resp. Ex. A, Tab 1.

[76] Julia Stowe et al., Bell's Palsy and Parenteral Inactivated Influenza Vaccine, 2 Hum. Vaccines 110 (2006).

[77] The Stowe et al. study used data from 1992 to 2005, and the articles does not reference H1N1 as included in the flu vaccines given those years in the UK. See Resp. Ex. A, Tab 2.

[78] Ali Rowhani-Rahbar et al., Immunization and Bell's Palsy in Children: A Case-Centered Analysis, 175 Am. J. Epidemiology 878 (2012).

2006. Resp. Ex. A, Tab 3 at 1-2.[79] Of the 822 children in the study, 233 received at least one vaccine in the 12 months prior to onset. Id. at 4. The authors found no association between vaccination (flu (trivalent), hepatitis B, or any vaccine) and Bell's palsy during their risk intervals of 1-14 days, 1-28 days, and 29-56 days. Id.

Wijnans et al.[80] did study a vaccine containing H1N1. Resp. Ex. A, Tab 4 at 1. The study population was comprised of all Bell's palsy cases using a primary health care database in the United Kingdom from 2009 to 2013. Id. at 1-2. They found a relative incidence rate of Bell's palsy between one and 42 days post-flu vaccination to be 0.88. Id. at 5. When adjusted for confounders, the relative incidence rate decreased to 0.85. Id. There was an increased risk of Bell's palsy on the day of [flu] vaccination," which the authors found to be "a likely opportunistic recording of cases." Id. at 6. However, the authors did not find evidence supporting an increased risk of Bell's palsy. Id. at 8.

Finally, Dr. Callaghan noted that the IOM[81] published a report in 2012 concluding that "[t]he evidence favors rejection of a causal relationship between inactivated [flu] vaccine and Bell's palsy." Resp. Ex. A, Tab 5 at 2; see also Tr. 128-29.[82] He added that all of Dr. Steinman's points to support the flu vaccination and Bell's palsy "ignore the robust epidemiologic evidence that there is no association between [flu] vaccination or any vaccination and Bell's palsy, [as] supported by the [IOM] 2012 report." Resp. Ex. A at 2; see also Tr. 126-27 (testifying that while the cause of Bell's palsy is unknown, vaccination is not part of the literature thought to be a causal mechanism and the epidemiologic studies above do not show an association between flu vaccine and Bell's palsy).

At the hearing and in his second report, Dr. Callaghan weighed in on Dr. Steinman's proposed theory, which he understood to be that there is "some homology between the [flu] vaccine and P2 and/or that the [flu] vaccine is capable of producing antibodies against gangliosides, and that therefore, [] led to Bell's palsy." Tr. 123; see also Resp. Ex. G at 1-3.

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[79] The H1N1 vaccine was first administered in the United States in 2009. H1N1, Vaccine Against 2009 H1N1 Influenza Virus, Ctrs. for Disease Control & Prevention, https://www.cdc.gov/h1n1flu/vaccination/public/vaccination_qa_pub.htm (last visited Oct. 20, 2023). There is no indication that it was administered to the patients in this study, conducted from 2001 to 2006.

[80] Leonoor Wijnans et al., Bell's Palsy and Influenza (H1N1)pdm09 Containing Vaccines: A Self-Controlled Case Series, 12 PLoS e0175539 (2017).

[81] Inst. of Med., Influenza Vaccine, in Adverse Effects of Vaccines: Evidence and Causality 293 (Kathleen Stratton et al. eds., 2012). This is also cited as Resp. Ex. C, Tab 5.

[82] The IOM study referenced two articles, Stowe et al. and Greene et al., and based on the information provided, it does not appear that these studies included vaccines containing the H1N1 virus, as it was not administered in the United States until 2009, outside of the years referenced in these studies. See Resp. Ex. A, Tab 5; Resp. Ex. A, Tab2.

Dr. Callaghan first took issue with Dr. Steinman's comparison of Bell's palsy and GBS. Tr. 123-24. He testified "GBS is a disease of . . . all the nerves in your body . . . whereas Bell's palsy is injury to one cranial nerve, so they're very different." Tr. 124. Additionally, he noted that "GBS can only be treated with IVIG and plasmapheresis which are not used for Bell's palsy." Tr. 127.

Dr. Callaghan testified that while Bell's palsy is a common mononeuropathy, the cause is currently unknown. Resp. Ex. G at 1; Tr. 117-18. Importantly, he pointed out that neither gangliosides nor P2 are known or thought to be part of the pathogenesis of Bell's palsy. Tr. 124. Regarding gangliosides, Dr. Callaghan testified that "there's not just one ganglioside. There are specific gangliosides, so [Dr. Steinman was] talking about a whole family of molecules," which, to Dr. Callaghan, did not make sense. Tr. 124-25. He testified that there is not a "strong link" between the flu vaccine and ganglioside antibodies. Tr. 125.

Regarding P2, Dr. Callaghan testified that the medical community does not know why people get Bell's palsy; they do not think that "there's antibodies or [the] immune system is triggered to attack P2 as part of the known pathogenies of Bell's palsy." Tr. 135. While Dr. Steinman relied on Abramsky et al. for the position that P2 is involved in Bell's palsy, Dr. Callaghan explained that in Abramsky et al., "P2 did not cause lymphocyte transformation in Bell's palsy patients in vitro whereas P1L did cause lymphocyte transformation." Resp. Ex. G at 2. Dr. Callaghan opined that in Abramsky et al., "there was no evidence to support Dr. Steinman's theory that P2 plays any role in the pathogenesis of Bell's palsy." Id. at 1; see also Tr. 229-30. Moreover, while Dr. Steinman alleged P1L was later renamed P2, Dr. Callaghan opined that "doesn't make sense" because both P1L and P2 were discussed and examined in Abramsky et al. and "P2 was negative in [Abramsky et al.] There was no response when trying to stimulate the lymphocytes from patients with Bell's palsy, whereas P1L [there] was." Resp. Ex. G at 2; Tr. 229. And according to Dr. Callaghan, the medical literature filed after the hearing to support Dr. Steinman's position "provide[d] no evidence or 'actual scientific facts' to support [Dr. Steinman's] claim that P1L was renamed P2." Resp. Ex. G at 2 (quoting Tr. 238).

Nonetheless, at the hearing, Dr. Callaghan agreed that there are "very small amounts of homology between the [flu] vaccine and P2." Tr. 125. But he opined that "showing homology at a few amino acids" does not link "molecular mimicry all the way from the [flu] vaccine to Bell's palsy." Tr. 125-26. Even if homology exists, Dr. Callaghan opined that would only be the first step. Tr. 126. The next step would be to "see that the patients have antibodies to both . . . the epitope that's supposed to be triggering this, in this case P2, [] against . . . the [flu] vaccine," and then have animal models which show "that this actually is the mechanism by which someone can get a disease such as Bell's palsy." Id. Dr. Callaghan opined "we have none of that here." Id.

ii. Althen Prongs Two and Three

Dr. Callaghan agreed, more likely than not, that Petitioner had Bell's palsy. Resp. Ex. G at 1; Tr. 114-15. However, he believed "there was a significant chance that Ramsay Hunt may be an alternative explanation due to [P]etitioner having symptoms that were not typical of a

seventh cranial nerve injury." Resp. Ex. G at 1; see also Tr. 114-15.[83] On cross-examination, however, Dr. Callaghan acknowledged that there was no indication Petitioner had a virus or infection. Tr. 134. Additionally, he opined that there is no relevancy to the fact that she was prescribed acyclovir. Tr. 137.

Regarding timing, Dr. Callaghan agreed with Dr. Steinman that Petitioner's Bell's palsy symptoms developed approximately 10 days after vaccination. Tr. 133-34. He conceded that "the timing is appropriate" based on the GBS literature. Id.

3. Respondent's Expert, J. Lindsay Whitton[84]

a. Background and Qualifications

Dr. Whitton received his B.Sc. in molecular biology, his M.B., Ch.B. in medicine, and his Ph.D. in herpesvirus transcription from the University of Glasgow in Scotland. Resp. Ex. D at 1. He also completed internships in medicine and surgery and has held various professor positions since 1986. Id.; Resp. Ex. C at 1. Dr. Whitton was involved as a researcher and professor at the Scripps Research Institute in California for approximately 38 years; but as of the date of the hearing, he was only serving as the Chair of the Appointments Promotions Committee. Tr. 149-51; Resp. Ex. D at 1. Dr. Whitton is a member of various professional societies and editorial boards and has authored or co-authored almost 200 publications. Resp. Ex. D at 1-15. Dr. Whitton does not provide patient care or diagnose or treat patients with Bell's palsy. Tr. 148, 158 (testifying that he is not licensed as a medical doctor); Resp. Ex. C at 2-3 (acknowledging that he cannot opine on the clinical aspects of the case).

b. Opinion

Dr. Whitton's opinions were focused on the association between the flu vaccine and Bell's palsy. He did not believe "the vaccine played any part at all" in Petitioner's development of Bell's palsy. Tr. 155, 194.

i. Althen Prong One

Dr. Whitton first noted that the etiology of Bell's palsy is often unclear, however, he acknowledged that potential causal mechanisms include inflammation and autoimmunity. Resp. Ex. C at 3; Tr. 197. He also testified that "facial paralysis can be triggered by virus infection, by varicella zoster virus." Tr. 157. And he opined the presentation of the disease "is strongly suggestive of a standard virus-mediated disease and not of an autoimmune reaction to the virus." Tr. 161.

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[83] The parties stipulated that Petitioner's diagnosis was Bell's palsy, not Ramsay Hunt syndrome. Joint Prehearing Submission at 1.

[84] Dr. Whitton submitted two expert reports in this matter and testified at the entitlement hearing. Resp. Exs. C, E; Tr. 145.

For molecular mimicry to occur, Dr. Whitton stated that at least two things must happen. Tr. 166. First, "the foreign antigen must induce an immune response." Id. He noted that it cannot be assumed "that the sequence in a protein or a ganglioside is always going to trigger an immune response." Id. Second, "the immune response, if it's induced, must be able to cross-react with or recognize a host component." Id. He emphasized that not every part of the host component, here as a protein or ganglioside, can trigger an immune response. Tr. 167. Dr. Whitton opined that "[t]he causation of disease by molecular mimicry is a third and entirely separate step." Id. He testified it is "fairly difficult" to cause disease via molecular mimicry and that molecular mimicry is not known to be a frequent cause of human disease. Tr. 169-70, 202; see also Resp. Ex. E at 9-10.

Dr. Whitton responded to both molecular mimicry theories presented by Dr. Steinman. Regarding the ganglioside theory, Dr. Whitton testified that there is "no evidence that gangliosides are involved in Bell's palsy." Tr. 173. While he admitted gangliosides are thought to be targets of autoimmunity in some cases of GBS, he agreed with Dr. Callaghan, that GBS and Bell's palsy are "very different," and he is not aware of "any evidence that says that immune response to gangliosides are involved in Bell's palsy." Tr. 170.

For support, he noted that the vaccines in Nachamkin et al., relied upon by Dr. Steinman, were grown from eggs, unlike the Flucelvax vaccine. Tr. 174. Moreover, Nachamkin et al. discussed GBS, not Bell's palsy. Tr. 172-74. He testified that Nachamkin et al. "suggested several ways in which the contents of [] flu vaccines grown in eggs might be able to trigger anti-ganglioside antibodies." Tr. 172. His understanding of how this might be done is "by transferring alien gangliosides, in other words, gangliosides from birds or gangliosides from the eggs." Id. Dr. Callaghan disagreed with Dr. Steinman's reliance on Nachamkin et al. because there is "no way that Flucelvax could have included avian gangliosides" because Flucelvax is grown in canine cells. Id.; see also Resp. Ex. C at 8 (opining there is "no possibility that Flucelvax . . . contains any avian gangliosides" (emphasis omitted)). Thus, he also disagreed with Dr. Steinman's opinion that "gangliosides are gangliosides." Tr. 172. Instead, Dr. Whitton referenced An et al. and opined that "[g]angliosides are glycosylated lipids. They're not glycosylated proteins." Tr. 173-74.

Additionally, Dr. Whitton cited Lei et al.[85] to support his position that there is no correlation with flu vaccination and the induction of antiganglioside antibodies. Resp. Ex. C at 7 (citing Resp. Ex. C, Tab 7). However, Lei et al. stated they "could not exclude the possibility that anti-GM1 antibodies might be generated rarely in [flu] vaccinees." Resp. Ex. C, Tab 7 at 5.

Regarding Dr. Steinman's P2 theory, Dr. Whitton first opined that, to his knowledge, "there's no association between P2 protein and Bell's palsy pathogenesis." Tr. 174, 192. Dr. Whitton rejected Dr. Steinman's three-step process supporting his molecular mimicry theory.

[85] Ting Lei et al., Anti-ganglioside Antibodies Were Not Detected in Human Subjects Infected with or Vaccinated Against 2009 Pandemic Influenza A (H1N1) Virus, 30 Vaccine 2605 (2012).

Resp. Ex. E at 5-7; Tr. 186; see also Tr. 168 (testifying one cannot reliably predict cross-reactivity).

First, he stated that BLAST searches were designed "to evaluate evolutionary relationships between proteins" not "to identify and predict immunological reactions." Tr. 175; see also Resp. Ex. C at 9. Thus, Dr. Whitton opined Dr. Steinman's BLAST searches are "very far" from being relevant; he deemed them "unsatisfactory" or "not useful." Resp. Ex. C at 8, 18; Tr. 200; see also Resp. Ex. E at 1.[86] Dr. Whitton opined that "none of Dr. Steinman's BLAST-identified homologies [met] or exceed[ed] the three Silvanovich [et al.] criteria, and the BLAST algorithm . . . itself tells us that the homologies [presented] [were] the result of chance." Resp. Ex. C at 11 (citing Resp. Ex. C, Tab 10; Resp. Ex. C, Tab 11);[87] see also Tr. 179.

According to Dr. Whitton, three criteria were recommended by Silvanovich et al. when using bioinformatic methods to evaluate protein sequence similarity and homology determinations for allergens. Tr. 179; see Resp. Ex. C at 10-11. Dr. Whitton opined that the first Silvanovich et al. criterion is that "the homology identified by BLAST must be at least 80 amino acids in length." Tr. 176. The second criterion is that "within those 80 amino acids, there must be a match, an identity of at least 28 amino acids, [or] 35 percent identity." Tr. 176-77. The third criterion is that the E-value[88] of the BLAST homology should be "about one in 10 million, around [] 10 to the minus seven [10^{-7}]." Tr. 177; see also Resp. Ex. C, Tab 11.[89] Dr. Whitton testified that Dr. Steinman's BLAST searches did not meet any of these criteria, and the E-values of Dr. Steinman's BLAST searches were "all one to 10 million-fold higher than that." Tr. 177. Therefore, Dr. Whitton concluded that the homologies were "undoubtedly the results of chance." Id.

In contrast, Dr. Steinman opined that the immune system interacts with shorter sequences of amino acids than outlined in Silvanovich et al.[90] See Tr. 214-18. Additionally, Silvanovich et al. applies in the contexts of allergens to determine the potential for allergy reactions (to assess

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[86] For a full and detailed explanation of Dr. Whitton's opinions about Dr. Steinman's use of BLAST searches, see Resp. Ex. C at 8-16; Resp. Ex. E at 1-7; Tr. 175-86, 224-27.

[87] Andre Silvanovich et al., The Use of E-Scores to Determine the Quality of Protein Alignments, 54 Regulatory Toxicology & Pharmacology S26 (2009).

[88] The E-value, or expect value, "is parameter that describes the number of hits one can 'expect' to see by chance when searching a database of a particular size. It decreases exponentially as the Score (S) of the match increases." Frequently Asked Questions, BLAST, Nat'l Libr. Med., https://blast.ncbi.nlm.nih.gov/doc/blast-help/FAQ.html (last visited Oct. 23, 2023).

[89] For a full and detailed explanation of Dr. Whitton's opinions of BLAST E-values, see Tr. 177-78, 224-27; Resp. Ex. C at 11.

[90] Dr. Steinman also testified that Silvanovich et al. is one reason why he starts with a BLAST search but that it is only the first step of his process. Tr. 94.

the safety of genetically modified crops). See Resp. Ex. C, Tab 11 at 1. In response, Dr. Whitton testified that the World Health Organization ("WHO") "approve[d] this approach for identification of allergens," and allergens trigger an immune response." Tr. 179. Thus, Dr. Whitton concluded that "the Silvanovich et al. criteria do apply to the immune response." Id.; see also Tr. 93-94.

Rather than applying the Silvanovich et al. criteria, Dr. Steinman used Lanz et al. and other literature to show the homology was significant. See Pet. Ex. 10 at 11. Lanz et al., published in 2022 with Dr. Steinman as a named author, "demonstrate[d] high-affinity molecular mimicry" between Epstein-Barr virus nuclear antigen1 and a central nervous system protein (GlialCAM). Pet. Ex. 76 at 1. The study also showed the functional relevance of their findings as it relates to multiple sclerosis. Id. Dr. Whitton criticized Dr. Steinman's reliance on Lanz et al. because they did not use a BLAST search to identify homology. Tr. 192. Moreover, he added that Lanz et al. is about Epstein-Barr virus and multiple sclerosis and therefore he argued that "both the alleged cause and the alleged outcome are different" than the case here. Tr. 188.

Relating back to Dr. Whitton's opinion that two things must happen for molecular mimicry to occur, Dr. Whitton conceded that step one, "the induction of immune response by that sequence of flu [hemagglutinin] . . . may be fulfilled" by the homology proposed by Dr. Steinman. Tr. 187; see also Tr. 166. Regarding step two, "which is the cross-recognition of the proposed target sequence in P2," Dr. Whitton opined "there is zero evidence presented for that." Tr. 187; see also Tr. 166.

Moreover, Dr. Whitton opined just because there is homology found in a BLAST search, does not mean there is molecular mimicry. Resp. Ex. C at 14; Tr. 182, 187.[91] He testified that "[y]ou will always find multiple homologies when you properly compare two proteins" and that most homologies do not trigger a biologic meaningful cross-reactive immune response. Tr. 182-85; see also Resp. Ex. C at 13-15 (opining that "the mere existence of homology is immunologically meaningless"). He explained that "[w]hen a foreign protein is injected into an animal, immune responses are made only to certain parts of the protein[,] not to each and every run of amino acids in the protein." Resp. Ex. C at 14 (emphasis omitted). Therefore, when a BLAST search "shows a homology between a foreign protein and a host protein, one cannot assume that the foreign part of the homology triggers any immune response whatsoever." Id. And even if an "imaginary immune response is induced by the foreign amino-acid sequence, one must not assume that that immune response can cross-react with the host part of the homology." Id. (emphasis omitted).

Finally, Dr. Whitton opined that "[t]he high incidence of Bell's palsy, together with the large number of flu vaccines administered annually, means that the temporal relationship between vaccination and disease is far more likely to be coincidental than causal." Resp. Ex. C

[91] For additional discussion by Dr. Whitton about why he disagreed with Dr. Steinman, see Resp. Ex. C at 15, Tr. 190-91, 201.

at 18; see also Tr. 193-94. Dr. Whitton cited Black et al.,[92] which "evaluated the likelihood of coincidental occurrence between flu vaccination and several neurological diseases including GBS." Resp. Ex. C at 17 (citing Resp. Ex. C, Tab 12). Relying on Black et al., he opined that given the incidence of GBS cases and the number of flu vaccines administered per year, the number of GBS cases within six weeks of vaccination is "purely by chance" and "coincidental." Id. Like Dr. Callaghan, Dr. Whitton also cited the 2012 IOM publication finding no evidence of increased risk of Bell's palsy after inactivated flu vaccination. Id. at 4 (citing Resp. Ex. A, Tab 5).

Ultimately, Dr. Whitton concluded that "neither gangliosides nor P2 protein are known to be potential targets in Bell's palsy." Tr. 203.

ii. Althen Prongs Two and Three

Dr. Whitton did not agree that there was a causational relationship between Petitioner's flu vaccination and the development of her Bell's palsy. Tr. 194. Specifically, he opined "the evidence . . . presented to support the contention that the flu vaccine administered on [September 21, 2017] was responsible for the signs/symptoms experienced by [Petitioner] is extremely weak." Resp. Ex. C at 17.

He noted Petitioner's treating physician initially ordered an antiviral, acyclovir, as a treatment for her Bell's palsy. Resp. Ex. C at 17 (citing Pet. Ex. 3 at 29). This is one reason that Dr. Whitton's believed that "medical personnel clearly considered viral infection as a likely cause" of her Bell's palsy. Id. However, Dr. Whitton did not opine, more likely than not, that Petitioner's Bell's palsy was caused by a viral infection. See id. at 1, 4-5.

Dr. Whitton agreed that Petitioner's onset of Bell's palsy was approximately 10 days after administration of the flu vaccine. Resp. Ex. C at 1; Tr. 194. He did not refute Dr. Steinman's opinion that the temporal association between vaccination and onset of Petitioner's Bell's palsy was appropriate given the theory of molecular mimicry.

4. Letter from Dr. Robert P. Lisak[93]

Dr. Lisak is a Professor of Neurology and Professor of Biochemistry, Microbiology and Immunology at Wayne State University School of Medicine. Pet. Ex. 92 at 2. He is also a Neurologist at Harper University Hospital and Detroit Receiving Hospital. Id. at 3. He has been involved in neuroimmunologic research, including the study of myelin basic proteins, since 1966. Pet. Ex. 91 at 1.

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[92] Steven Black et al., Importance of Background Rates of Disease in Assessment of Vaccine Safety During Mass Immunisation with Pandemic H1N1 Influenza Vaccines, 374 Pub. Health 2115 (2009).

[93] Dr. Lisak did not testify at the hearing.

Petitioner submitted a letter by Dr. Lisak after the hearing to comment on the P1 and P2 myelin protein nomenclature issue. Pet. Ex. 91 at 1. He supported Dr. Steinman's position regarding the "evolution of the terminology of the [peripheral nervous system] myelin basic protein" and that the P1L protein referenced in Abramsky et al. is now called P2. Id. Dr. Lisak explained that

> [t]he original terminology of P1L and P2(L) in the Abramsky [et al.] papers is known to be incorrect. It is known and widely accepted since the late 1970s that P1L is the P2 protein used in all the other papers Dr. Steinman cited, as well as in [his own] studies[94] . . . and that of others, induces [EAN] and is specific to the [peripheral nervous system]. What Abramsky [et al.] termed P2 (L) is actually P1 . . . that is identical to [myelin basic protein] the constituent of CNS that induces [EAE]. The use of the name P2 myelin protein is the correct term for the [peripheral nervous system] myelin specific protein being studied in EAN and studies of human serum and lymphocyte reactivity in diseases.

Id.

IV. DISCUSSION

A. Standards for Adjudication

The Vaccine Act was established to compensate vaccine-related injuries and deaths. § 10(a). "Congress designed the Vaccine Program to supplement the state law civil tort system as a simple, fair and expeditious means for compensating vaccine-related injured persons. The Program was established to award 'vaccine-injured persons quickly, easily, and with certainty and generosity.'" Rooks v. Sec'y of Health & Hum. Servs., 35 Fed. Cl. 1, 7 (1996) (quoting H.R. Rep. No. 908 at 3, reprinted in 1986 U.S.C.C.A.N. at 6287, 6344).

Petitioner's burden of proof is by a preponderance of the evidence. § 13(a)(1). The preponderance standard requires a petitioner to demonstrate that it is more likely than not that the vaccine at issue caused the injury. Moberly v. Sec'y of Health & Hum. Servs., 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010). Proof of medical certainty is not required. Bunting v. Sec'y of Health & Hum. Servs., 931 F.2d 867, 873 (Fed. Cir. 1991). Petitioner need not make a specific type of evidentiary showing, i.e., "epidemiologic studies, rechallenge, the presence of pathological markers or genetic predisposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." Capizzano v. Sec'y of Health & Hum. Servs., 440 F.3d 1317, 1325 (Fed. Cir. 2006). Instead, Petitioner may satisfy her burden by presenting circumstantial evidence and reliable medical opinions. Id. at 1325-26.

In particular, Petitioner must prove that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." Moberly, 592 F.3d at 1321 (quoting Shyface v. Sec'y of Health & Hum. Servs., 165 F.3d 1344, 1352-53 (Fed. Cir. 1999));

[94] Dr. Lisak referenced papers numbered 90, 92, 115, and 120 from his CV, however those were not filed. Pet. Ex. 91 at 1; see Pet. Ex. 92 at 23-24.

see also Pafford v. Sec'y of Health & Hum. Servs., 451 F.3d 1352, 1355 (Fed. Cir. 2006). The received vaccine, however, need not be the predominant cause of the injury. Shyface, 165 F.3d at 1351. A petitioner who satisfies this burden is entitled to compensation unless Respondent can prove, by a preponderance of the evidence, that the vaccinee's injury is "due to factors unrelated to the administration of the vaccine." § 13(a)(1)(B). However, if a petitioner fails to establish a prima facie case, the burden does not shift. Bradley v. Sec'y of Health & Hum. Servs., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

"Regardless of whether the burden ever shifts to the [R]espondent, the special master may consider the evidence presented by the respondent in determining whether the [P]etitioner has established a prima facie case." Flores v. Sec'y of Health & Hum. Servs., 115 Fed. Cl. 157, 162-63 (2014); see also Stone v. Sec'y of Health & Hum. Servs., 676 F.3d 1373, 1379 (Fed. Cir. 2012) ("[E]vidence of other possible sources of injury can be relevant not only to the 'factors unrelated' defense, but also to whether a prima facie showing has been made that the vaccine was a substantial factor in causing the injury in question."); de Bazan v. Sec'y of Health & Hum. Servs., 539 F.3d 1347, 1353 (Fed. Cir. 2008) ("The government, like any defendant, is permitted to offer evidence to demonstrate the inadequacy of the [P]etitioner's evidence on a requisite element of the [P]etitioner's case-in-chief."); Pafford, 451 F.3d at 1358-59 ("[T]he presence of multiple potential causative agents makes it difficult to attribute 'but for' causation to the vaccination. . . . [T]he Special Master properly introduced the presence of the other unrelated contemporaneous events as just as likely to have been the triggering event as the vaccinations.").

B. Causation

To receive compensation through the Program, Petitioner must prove either (1) that she suffered a "Table Injury"—i.e., an injury listed on the Vaccine Injury Table—corresponding to a vaccine that she received, or (2) that she suffered an injury that was actually caused by a vaccination. See §§ 11(c)(1), 13(a)(1)(A); Capizzano, 440 F.3d at 1319-20. Because Petitioner does not allege she suffered a Table Injury, she must prove a vaccine she received caused her injury. To do so, Petitioner must establish, by preponderant evidence: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." Althen, 418 F.3d at 1278.

The causation theory must relate to the injury alleged. Petitioner must provide a sound and reliable medical or scientific explanation that pertains specifically to this case, although the explanation need only be "legally probable, not medically or scientifically certain." Knudsen v. Sec'y of Health & Hum. Servs., 35 F.3d 543, 548-49 (Fed. Cir. 1994). Petitioner cannot establish entitlement to compensation based solely on her assertions; rather, a vaccine claim must be supported either by medical records or by the opinion of a medical doctor. § 13(a)(1). In determining whether Petitioner is entitled to compensation, the special master shall consider all material in the record, including "any . . . conclusion, [or] medical judgment . . . which is contained in the record regarding . . . causation." § 13(b)(1)(A). The undersigned must weigh the submitted evidence and the testimony of the parties' proffered experts and rule in Petitioner's favor when the evidence weighs in her favor. See Moberly, 592 F.3d at 1325-26 ("Finders of fact are entitled—indeed, expected—to make determinations as to the reliability of the evidence

presented to them and, if appropriate, as to the credibility of the persons presenting that evidence."); Althen, 418 F.3d at 1280 (noting that "close calls" are resolved in Petitioner's favor).

Testimony that merely expresses the possibility—not the probability—is insufficient, by itself, to substantiate a claim that such an injury occurred. See Waterman v. Sec'y of Health & Hum. Servs., 123 Fed. Cl. 564, 573-74 (2015) (denying Petitioner's motion for review and noting that a possible causal link was not sufficient to meet the preponderance standard). The Federal Circuit has made clear that the mere possibility of a link between a vaccination and a petitioner's injury is not sufficient to satisfy the preponderance standard. Moberly, 592 F.3d at 1322 (emphasizing that "proof of a 'plausible' or 'possible' causal link between the vaccine and the injury" does not equate to proof of causation by a preponderance of the evidence); Boatmon v. Sec'y of Health & Hum. Servs., 941 F.3d 1351, 1359-60 (Fed. Cir. 2019). While certainty is by no means required, a possible mechanism does not rise to the level of preponderance. Moberly, 592 F.3d at 1322; see also de Bazan, 539 F.3d at 1351.

V. ANALYSIS

A. Althen Prong One

Under Althen prong one, Petitioner must set forth a medical theory explaining how the received vaccine could have caused the sustained injury. Andreu v. Sec'y of Health & Hum. Servs., 569 F.3d 1367, 1375 (Fed. Cir. 2009); Pafford, 451 F.3d at 1355-56. Petitioner's theory of causation need not be medically or scientifically certain, but it must be informed by a "sound and reliable" medical or scientific explanation. Boatmon, 941 F.3d at 1359; see also Knudsen, 35 F.3d at 548; Veryzer v. Sec'y of Health & Hum. Servs., 98 Fed. Cl. 214, 223 (2011) (noting that special masters are bound by both § 13(b)(1) and Vaccine Rule 8(b)(1) to consider only evidence that is both "relevant" and "reliable"). If Petitioner relies upon a medical opinion to support her theory, the basis for the opinion and the reliability of that basis must be considered in the determination of how much weight to afford the offered opinion. See Broekelschen v. Sec'y of Health & Hum. Servs., 618 F.3d 1339, 1347 (Fed. Cir. 2010) ("The special master's decision often times is based on the credibility of the experts and the relative persuasiveness of their competing theories."); Perreira v. Sec'y of Health & Hum. Servs., 33 F.3d 1375, 1377 n.6 (Fed. Cir. 1994) (stating that an "expert opinion is no better than the soundness of the reasons supporting it" (citing Fehrs v. United States, 620 F.2d 255, 265 (Ct. Cl. 1980))).

The undersigned finds Petitioner has set forth a sound and reliable medical theory, molecular mimicry, to explain how the flu vaccine can cause Bell's palsy.

Moreover, the medical literature and the testimony and opinions of Dr. Steinman show that there is persuasive evidence of the similarity between GBS and Bell's palsy, that Bell's palsy is a variant of GBS, and that molecular mimicry is an appropriate causal mechanism of GBS and Bell's palsy. Further, the literature provides support for Dr. Steinman's opinion that Bell's palsy is caused by molecular mimicry.

Greco et al. provides a comprehensive analysis of the relevant immunological theories of causation in Bell's palsy, specifically molecular mimicry. The authors state, "[s]ome evidence implicates the involvement of immune mechanisms in Bell's palsy. Many reports have indicated the association between facial paralysis and [GBS], a condition that was recently shown to be a cell mediated, autoimmune neuritis." Pet. Ex. 19 at 4. The authors also discuss Abramsky et al., which Dr. Steinman relies upon to show homology between the flu vaccine and human basic protein (P1L, now P2L) of peripheral nerve myelin in patients with Bell's palsy. Abramsky et al. also suggests that "cell-mediated autoimmune mechanisms may be of importance in the pathogenesis of Bell's palsy." Id.; see also Pet. Ex. 20 at 1. Bell's palsy, like GBS, is an acute demyelinating disease of the peripheral nervous system. There is a body of evidence showing there is an immune-mediated causal theory that is sound and reliable, and the most likely of the relevant immune-mediated mechanisms is molecular mimicry. Thus, the undersigned finds that Petitioner has provided sound and reliable evidence for the application of molecular mimicry in the context of Bell's palsy.

Molecular mimicry has been accepted as a sound and reliable theory in many demyelinating conditions, including GBS, in the Vaccine Program, forming the basis for petitioners to be entitled to compensation. See, e.g., Conte v. Sec'y of Health & Hum. Servs., No. 17-403V, 2020 WL 5743696, at *57 (Fed. Cl. Spec. Mstr. July 27, 2020) (noting the theory of molecular mimicry in a GBS case is "well-established and well-settled in the Vaccine Program"); Barone v. Sec'y of Health & Hum. Servs., No. 11-707V, 2014 WL 6834557, at *8-9 (Fed. Cl. Spec. Mstr. Nov. 12, 2014) (noting molecular mimicry "has been accepted in other Program cases as a reliable medical explanation for how various autoimmune conditions could develop after the receipt of different kinds of vaccinations"); Larson v. Sec'y of Health & Hum. Servs., No. 16-633V, 2023 WL 3765631 (Fed. Cl. Spec. Mstr. June 1, 2023), mot. for review denied, 2023 WL 6387783 (Fed. Cl. Oct. 2, 2023); Maloney v. Sec'y of Health & Hum. Servs., No. 19-1713V, 2022 WL 1074087 (Fed. Cl. Spec. Mstr. Mar. 17, 2022).[95]

Petitioner also provided preponderant evidence, by expert opinion and medical literature, of an association between the flu vaccine and Bell's palsy. Zhou et al. concluded there "may be a signal of possible association between [flu] vaccines and an increased risk of Bell's palsy." Pet. Ex. 47 at 5. Bardage et al. reported "a significantly increased risk for Bell's palsy" in "those vaccinated in the early phase of the vaccination campaign (≤ 45 days), when high risk groups predominated." Pet. Ex. 41 at 4. Kamath et al. noted that reports of Bell's palsy were higher after receipt of the flu vaccination as compared to other vaccines. Pet. Ex. 70 at 4-6. Lastly, Huang et al. concluded there was an increased risk of Bell's palsy after the H1N1 vaccination. Pet. Ex. 69 at 2.

The lack of epidemiological evidence is not dispositive. It is difficult to use epidemiology to determine whether a vaccine is implicated in causation. Because while adverse reactions like this do not appear in the epidemiological evidence cited by Respondent's experts, it may be that events are too rare to be captured. Moreover, "[r]equiring epidemiologic studies . .

[95] The undersigned acknowledges that the last case in this string cite involves a different vaccine, although the same illness and general theory.

. or general acceptance in the scientific or medical communities . . . impermissibly raises a claimant's burden under the Vaccine Act and hinders the system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants." Andreu, 569 F.3d at 1378 (quoting Capizzano, 440 F.3d at 132-26); see also Althen, 418 F.3d at 1280 (noting that "close calls" are resolved in Petitioner's favor). The undersigned does not find the epidemiological literature to be definitive or determinative in this regard.

The undersigned also finds that there is scientific support for Dr. Steinman's two theories that illustrate how molecular mimicry could cause Bell's palsy. Dr. Steinman has identified components of the flu vaccine that could initiate the development of antibodies that could cross-react with peripheral nerve myelin and trigger an autoimmune response.

His first theory is based on ganglioside mimicry. Greco et al. provides foundational support by showing that human cranial nerves are composed of gangliosides. Nachamkin et al. shows that ganglioside antibodies (from *C. jejuni* infection) are found in patients with GBS. Nachamkin et al. also provides evidence that flu vaccines, including those containing H1N1, induce antibody responses to anti-gangliosides (anti-GM1) and to hemagglutinin (found in the 2017-2018 vaccine, Flucelvax). An et al. shows that the flu vaccine grown in canine kidney cells (used in Flucelvax) could glycosylate flu vaccine proteins, like the egg-based vaccines studied by Nachamkin et al.

Thus, Dr. Steinman produced literature to show that Bell's palsy involves the cranial nerves, and that gangliosides are found in these nerves. He has shown that patients with GBS, and Miller Fisher (a variant of GBS which involves cranial nerves) have anti-ganglioside antibodies. Next, he has shown that flu vaccines (H1N1) induce antibody responses. And he establishes the flu vaccine at issue here, although grown in canine kidney cells, glycosylates flu vaccine protein like its egg-based counterpart. For each aspect of his theory, Petitioner has provided scientific support through medical literature.

There is also evidence to support Dr. Steinman's second theory based on the P2 protein in myelin in the peripheral nerves. Abramsky et al. found a "defined in vitro response to a human basic protein" (P1L) of peripheral nerve myelin in patients with Bell's palsy and suggested that molecular mimicry may play a causal role. Pet. Ex. 20 at 4. Dr. Steinman provides preponderant evidence that the nomenclature has changed, and that that P1L is now referenced as P2.[96] The P2 protein may be specific to the peripheral nerve myelin, targeted in Bell's palsy. Dr. Steinman then uses a three-step process to identify protein sequences that could implicate molecular mimicry between the flu vaccine and P2.

Petitioner need not make a specific type of evidentiary showing or require identification of homology to prove that molecular mimicry is a sound and reliable theory by preponderant evidence. Given the state of current scientific knowledge, there is no way that a petitioner could

[96] Assuming the undersigned's ruling on this point is in error, it does not change the ruling in favor of entitlement, as this issue is not determinative of the outcome, in that Dr. Steinman provides an alternative mechanistic theory (gangliosides) which is sound and reliable.

satisfy such a requirement. Further, requiring proof of specific homology or proof of identical protein sequences between the flu vaccine and the peripheral nervous system to prove causation would require scientific certainty, which is a bar too high. See Knudsen, 35 F.3d at 549 (explaining that "to require identification and proof of specific biological mechanisms would be inconsistent with the purpose and nature of the vaccine compensation program").

Regarding Dr. Steinman's testimony about homologous sequences, the undersigned finds that he was illustrating how molecular mimicry can cause Bell's palsy using readily available resources. Dr. Steinman explained that he could not perform research on Petitioner. He also explained the limitations of the process that he used. The undersigned will not reject the mechanistic theory of molecular mimicry because Dr. Steinman was unable to prove his theory in a laboratory. The undersigned is not willing to disregard applicable medical literature, or ignore her knowledge and experience about the application of molecular mimicry in the context of demyelinating peripheral neuropathies, when molecular mimicry has been repeatedly shown by preponderant evidence to be a sound and reliable theory in the context of vaccine causation.

Lastly, the undersigned's finding is consistent with her prior ruling involving the flu vaccine and Bell's palsy. See E. A. v. Sec'y of Health & Hum. Servs., No. 18-1587V, 2023 WL 2640710 (Fed. Cl. Spec. Mstr. Jan. 24, 2023). In E.A., the Petitioner received a flu vaccination on October 19, 2015. Id. at *4, *29. Approximately forty days post-vaccination, she awoke with left facial numbness and weakness. Id. Examination revealed weakness of the seventh cranial nerve. Id. She was diagnosed with Bell's palsy. Id. Petitioner's expert opined that molecular mimicry was the most likely mechanism, and he explained that components of the vaccine can lead to autoimmune responses directed against the facial nerve triggering demyelination and resulting in neuropathy. Id. at *19, *27-28. The experts cited many of the same articles and advanced many of the same arguments for and against causation that were discussed herein. Id. at *14-25, *27-28. The undersigned found that the Petitioner in E.A. had provided preponderant evidence of a sound and reliable causal theory, satisfying Althen prong one. Id. at *28. The undersigned again evaluates the same evidence here, and comes to the same conclusion.

For the reasons discussed above, the undersigned finds that Petitioner has provided preponderant evidence of a sound and reliable causal theory, satisfying Althen prong one.

B. Althen Prong Two

Under Althen prong two, Petitioner must prove by a preponderance of the evidence that there is a "logical sequence of cause and effect showing that the vaccination was the reason for the injury." Capizzano, 440 F.3d at 1324 (quoting Althen, 418 F.3d at 1278). "Petitioner must show that the vaccine was the 'but for' cause of the harm . . . or in other words, that the vaccine was the 'reason for the injury.'" Pafford, 451 F.3d at 1356 (internal citations omitted).

In evaluating whether this prong is satisfied, the opinions and views of the vaccinee's treating physicians are entitled to some weight. Andreu, 569 F.3d at 1367; Capizzano, 440 F.3d at 1326 ("[M]edical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury.'" (quoting Althen,

418 F.3d at 1280)). Medical records are generally viewed as trustworthy evidence, since they are created contemporaneously with the treatment of the vaccinee. Cucuras v. Sec'y of Health & Hum. Servs., 993 F.2d 1525, 1528 (Fed. Cir. 1993). The Petitioner need not make a specific type of evidentiary showing, i.e., "epidemiologic studies, rechallenge, the presence of pathological markers or genetic predisposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." Capizzano, 440 F.3d at 1325. Instead, Petitioner may satisfy her burden by presenting circumstantial evidence and reliable medical opinions. Id. at 1325-26.

Regarding Althen prong two, the undersigned finds there is no issue regarding diagnosis, as the parties agree that Petitioner had Bell's palsy. This diagnosis is well supported by the medical records and the opinions of the treating physicians.

Further, the undersigned finds that Petitioner provided preponderant evidence of a logical sequence of cause and effect showing that her vaccination was the cause of her Bell's palsy. First, Petitioner's clinical course is consistent with the medical literature and case reports of Bell's palsy following vaccination.

Petitioner received the flu vaccine on September 21, 2017, and 13 days later, on October 4, presented to her physician with difficulty closing her eye, drooping eye, facial muscle weakness, and ear pain. Physical examination revealed palsy of the facial nerve (seventh cranial nerve). An MRI was done without contrast and did not reveal abnormalities. Although Petitioner did not have MRI findings that specifically showed enhancement of the cranial nerve or a specific demyelinating process, she did have abnormal findings of the seventh cranial nerve on neurological examination.

Further, the undersigned finds no evidence of any alternative cause. There is no evidence in the record to suggest that Petitioner had varicella zoster. Physical examination did not reveal any vesicles, rash, or lesions consistent with varicella zoster. She also did not test positive for Lyme disease. Dr. Callaghan acknowledges that there was no indication of a virus or infection. While Dr. Whitton opines Petitioner's "medical personnel clearly considered viral infection as a likely cause" because they prescribed acyclovir, there were no signs of infection on examination. Resp. Ex. C at 17. And Dr. Callaghan opines that the prescription of acyclovir had no relevance.

It is important to note that Dr. Whitton is not licensed as a medical doctor, and he testified that he does not diagnose or treat patients who have neurological illnesses, like Bell's palsy. Thus, he has not determined whether a patient's Bell's palsy was caused by infection or vaccination. While Dr. Whitton is eminently qualified to opine in the area of his expertise—immunology and microbial science—the undersigned finds that his opinions as to diagnosis and/or alternate cause carry less weight, especially given his testimony acknowledging that he could not opine on the clinical aspects of the case. Tr. 158; Resp. Ex. C at 2-3.

Dr. Callaghan, who is a medical doctor (neurologist), did not offer an opinion that infection caused Petitioner's Bell's palsy. Because Dr. Callaghan is well qualified to opine on diagnosis and the etiology of that diagnosis by virtue of his training, experience, and qualifications, the undersigned finds his opinions more persuasive. In weighing the

persuasiveness of opinion testimony, special masters may consider the relative expertise, backgrounds, and specialties of the experts. Locane v. Sec'y of Health & Hum. Servs., 685 F.3d 1375, 1380 (Fed. Cir. 2012); Stone, 676 F.3d at 1382 (noting the special master correctly found one experts testimony on an issue to be more reliable than the others due to "more extensive and more recent experience"); Pafford, 451 F.3d at 1359 (affirming the special master's rejection of expert's testimony because he lacked proper qualifications in the specialty areas in which he testified); see also Dwyer v. Sec'y of Health & Hum. Servs., No. 03-1202V, 2010 WL 892250, at *64 (Fed. Cl. Spec. Mstr. Mar. 12, 2010) (giving greater weight to M.D. epidemiologists' opinions on medical issues than to Ph.D. epidemiologist's opinion). The undersigned acknowledges the Circuit Court's directive, and here, Dr. Whitton agrees that the clinical issues, which include the question of alternative causes, is outside of his expertise. The question of whether Petitioner's Bell's palsy was caused by an alternative cause like infection involves the practice of medicine, which requires specific training, experience, and qualifications, and in general, experience in caring for patients.

Moreover, Dr. Whitton fails to state his opinion as to alternate cause to a reasonable degree of probability. He opines that because Petitioner's treating physicians ordered an antiviral medication, acyclovir, that they considered "viral infection as a likely cause." Resp. Ex. C at 17. However, he does not express the opinion, more likely than not, that a viral infection was the cause of Petitioner's Bell's palsy. Accordingly, the undersigned finds that Dr. Whitton's opinion does not carry sufficient weight to support alternative causation.

Thus, the undersigned finds that Petitioner provided preponderant evidence of a logical sequence of cause and effect, satisfying Althen prong two.

C. Althen Prong Three

Althen prong three requires Petitioner to establish a "proximate temporal relationship" between the vaccination and the injury alleged. Althen, 418 F.3d at 1281. That term has been defined as a "medically acceptable temporal relationship." Id. The Petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disease's etiology, it is medically acceptable to infer causation-in-fact." de Bazan, 539 F.3d at 1352. The explanation for what is a medically acceptable time frame must also coincide with the theory of how the relevant vaccine can cause the injury alleged (under Althen Prong One). Id.; Koehn, 773 F.3d at 1243; Shapiro v. Sec'y of Health & Hum. Servs., 101 Fed. Cl. 532, 542 (2011), recons. den'd after remand, 105 Fed. Cl. 353 (2012), aff'd mem., 503 F. App'x 952 (Fed. Cir. 2013).

The parties stipulate, and the experts agree, that Petitioner received the flu vaccine on September 21, 2017, and approximately 10 days later, on October 1, 2017, she developed Bell's palsy. Dr. Steinman opines that 10 days is appropriate given the purported autoimmune mechanism of molecular mimicry. He also provides medical literature which shows onset ranges from one to 30 days (Zhou et al.), three to 10 days (Chou et al.), and zero to 42 days (Huang et al.). Moreover, Respondent's experts do not provide evidence refuting Dr. Steinman's opinion that there was an appropriate temporal association between vaccination and the onset of Petitioner's Bell's palsy.

Therefore, Petitioner has provided preponderant evidence satisfying Althen prong three.

D. Alternative Causation

Because the undersigned concludes that Petitioner established a prima facie case, Petitioner is entitled to compensation unless Respondent can put forth preponderant evidence "that Petitioner's injury was in fact caused by factors unrelated to the vaccine." Whitecotton v. Sec'y of Health & Hum. Servs., 17 F.3d 374, 376 (Fed. Cir. 1994), rev'd on other grounds sub nom., Shalala v. Whitecotton, 514 U.S. 268 (1995); see also Walther v. Sec'y of Health & Hum. Servs., 485 F.3d 1146, 1151 (Fed. Cir. 2007). As discussed above in the Althen prong two analysis, the undersigned found Respondent failed to establish evidence to show that Petitioner's Bell's palsy was caused by a source other than vaccination. Thus, Respondent did not prove by a preponderance of evidence that Petitioner's injury is "due to factors unrelated to the administration of the vaccine." § 13(a)(1)(B).

VI. CONCLUSION

For the reasons discussed above, the undersigned finds that Petitioner has established by preponderant evidence that her flu vaccine caused her Bell's palsy. Therefore, Petitioner is entitled to compensation. A separate damages order will issue.

IT IS SO ORDERED.

s/Nora Beth Dorsey
Nora Beth Dorsey
Special Master